



STIC Search Report

Biotech-Chem Library

STIC Database Tracking Number: 199240

TO: Devesh Khare
Location: rem/5C35/5C18
Art Unit: 1623
Friday, August 25, 2006
Case Serial Number: 10/632875

From: Saloni Sharma
Location: Biotech-Chem Library
REM-1A64
Phone: (571)272-8601

saloni.sharma@uspto.gov

Search Notes

Examiner Khare,

See attached results.

If you have any questions about this search feel free to contact me at any time.

Thank you for using STIC search services!

Saloni Sharma
Technical Information Specialist
STIC Biotech/Chem Library
(571)272-8601

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STIC SEARCH RESULTS FEEDBACK FORM

Biotech-Chem Library

Questions about the scope or the results of the search? Contact *the searcher or contact*:

Mary Hale, Information Branch Supervisor
571-272-2507 Remsen E01 D86

Voluntary Results Feedback Form

➤ I am an examiner in Workgroup: Example: 1610

➤ Relevant prior art **found**, search results used as follows:

- ☐ 102 rejection
- ☐ 103 rejection
- ☐ Cited as being of interest.
- ☐ Helped examiner better understand the invention.
- ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
(journal articles, conference proceedings, new product announcements etc.)

➤ Relevant prior art **not found**:

- ☐ Results verified the lack of relevant prior art (helped determine patentability).
- ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC/Biotech-Chem Library Remsen Bldg.

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8-1035

199240

M9

STIC-Biotech/ChemLib

From: Khare, Devesh
Sent: Monday, August 21, 2006 3:48 PM
To: STIC-Biotech/ChemLib
Subject: 10/632,875: Please provide a structure search. Claim and hints attached with request form.
Thank you.



claims.doc SEARCH.REQ
1.doc

Devesh Khare, J.D., Ph.D.
Patent Examiner -Art Unit 1623
United States Patent & Trademark Office
Washington, DC.
571-272-0653; Devesh.Khare@USPTO.GOV

Searcher: *Salim Khan*
Searcher Phone: _____
Date Searcher Picked up: 8/24/06
Date completed: 8/25/06
Searcher Prep Time: 80
Online Time: 70

Type of Search
NA# _____ AA# _____
S/L: _____ Oligomer: _____
Encode/Transl: _____
Structure #: _____ Text: _____
Inventor: _____ Litigation: _____

Vendors and cost where applicable
STN: 1
DIALOG: _____
QUESTEL/ORBIT: _____
LEXIS/NEXIS: _____
SEQUENCE SYSTEM: _____
WWW/Internet: _____
Other (Specify): _____

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Access DB# _____

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's full Name: Devesh Khare Examiner #: 77931 Date: 08/21/2006

Art Unit: 1623 Phone Number 272-0653 Serial Number: 10/632,875

Mail Box: Remsen 5C18 and Bldg/Room Location: 5C35 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be search Include the elected species or structures, key words, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: 2',3'-dideoxynucleoside analogues for the treatment or prevention of Flaviviridae infections.

Inventors (please provide full names): Raymond F. Schinazi, Robert Striker and Junxing Shi.

Earliest priority Filing Date: 08/01/2002

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please carry out a search on the attached claims sheet; examiner's hints provided.

Thank you.

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Searcher: _____
Searcher Phone #: _____
Searcher Location: _____
Date Searcher Picked Up: _____
Date Completed: _____
Searcher Prep & Review Time: _____
Clerical prep time: _____
Online Time: _____

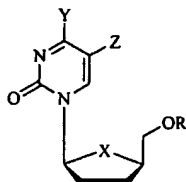
Type of Search
NA Sequence (#) _____
AA Sequence (#) _____
Structure (#) _____
Bibliographic _____
Litigation _____
Fulltext _____
Patent Family _____
Other _____

Vendors and cost where applicable
STN _____
Dialog _____
Questel/Orbit _____
Dr. Link _____
Lexis/Nexis _____
Sequence Systems _____
WWW/Internet _____
Other (specify) _____

PTO-1590 (1-2000)

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31. A pharmaceutical composition for the treatment and/or prophylaxis of an HCV infection in a host, comprising an effective treatment amount of a 2',3'-dideoxynucleoside of the formula:



or a pharmaceutically acceptable salt or prodrug thereof, wherein

- (i) X is O, S, S=O, SO₂, NR¹, N⁺R¹R², CH₂, CHF or CR³R⁴;

R¹ and R² are independently hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, or C₃₋₈ cycloalkyl;

R³ and R⁴ are independently hydrogen, halogen (F, Cl, Br, or I), OH or OR⁵;

R⁵ is hydrogen or a hydroxyl protecting group such as alkyl, acyl or silyl;

- (ii) Y is NH₂, NHR⁶, NR⁶R⁷, OH or OR⁸

each R⁶, R⁷ and R⁸ is independently H, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₈ cycloalkyl, cyclopropyl, or C₂₋₆ acyl;

- (iii) Z is chosen from hydrogen, halogen (F, Cl, Br, or I), C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, CN, CF₃, N₃, NO₂, aryl, heteroaryl and COR⁹;

R⁹ is chosen from H, OH, SH, C₁₋₆ alkyl, C₁₋₆ aminoalkyl, C₁₋₆ alkoxy and C₁₋₆ thioalkyl; and

- (iv) R is hydrogen, phosphate; acyl; -C(O)R¹⁰, alkyl; sulfonate ester; sulfonyl; a lipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group, which, when administered *in vivo*, is capable of providing a compound wherein R is H or phosphate;

R¹⁰ is a C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, aryl, monophosphate, diphosphate, triphosphate, or -P(O)(OR¹¹)₂;

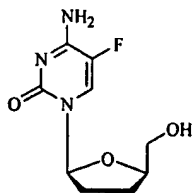
each R¹¹ is independently hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl or a hydroxyl-protecting group;

together with pharmaceutically acceptable carrier.

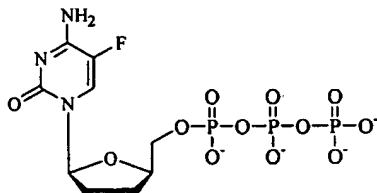
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Examiner's hints and search points:

In one preferred embodiment, the active compound is β -L-2',3'-dideoxy-5-fluorocytidine (also referred to as β -L-ddFC), of the structure:

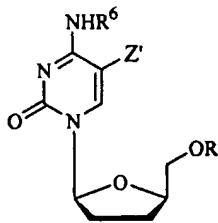


In one embodiment, the active compound is β -L-2',3'-dideoxy-5-fluorocytidine triphosphate (also referred to as β -L-ddFC-TP), of the structure:



or a pharmaceutically acceptable salt or prodrug thereof.

In an alternate embodiment, the active compound is β -L-2',3'-dideoxy-5-substituted-cytidine, of the structure:



or a pharmaceutically acceptable salt thereof, wherein

Note: Z' and R groups are same as Z and R groups shown in the claim above.

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(FILE 'HOME' ENTERED AT 10:01:20 ON 25 AUG 2006)

FILE 'CAPLUS' ENTERED AT 10:01:41 ON 25 AUG 2006

E US2003-632875/APPS

L1 2 SEA ABB=ON PLU=ON US2003-632875/AP
D SCAN

FILE 'REGISTRY' ENTERED AT 10:06:09 ON 25 AUG 2006

L2 STRUCTURE UPLOADED

D QUE L2

L3 50 SEA SSS SAM L2

L4 109180 SEA SSS FUL L2

SAVE L4 KHARE875/A TEMP

FILE 'CAPLUS' ENTERED AT 10:07:52 ON 25 AUG 2006

L5 94725 SEA ABB=ON PLU=ON L4
SEL RN L1

FILE 'REGISTRY' ENTERED AT 10:08:33 ON 25 AUG 2006

L6 166 SEA ABB=ON PLU=ON (119567-79-2/BI OR 121154-51-6/BI OR
147058-39-7/BI OR 198153-51-4/BI OR 206269-27-4/BI OR 220581-49
-7/BI OR 223603-41-6/BI OR 254750-02-2/BI OR 36791-04-5/BI OR
402957-28-2/BI OR 472960-22-8/BI OR 56-92-8/BI OR 62304-98-7/BI
OR 768-94-5/BI OR 10380-93-5/BI OR 107-20-0/BI OR 107036-57-7/
BI OR 108-24-7/BI OR 118390-30-0/BI OR 128075-94-5/BI OR
128112-71-0/BI OR 15083-05-3/BI OR 150938-53-7/BI OR 150938-54-
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6/BI OR 2022-85-7/BI OR 221156-18-9/BI OR 24259-59-4/BI OR
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4137-57-9/BI OR 415704-30-2/BI OR 51172-83-9/BI OR 52813-63-5/B
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57071-82-6/BI OR 57901-59-4/BI OR 57901-63-0/BI OR 57901-65-2/B
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656809-04-0/BI OR 656809

L7 31 SEA ABB=ON PLU=ON L6 AND L4
D SCAN

FILE 'CAPLUS' ENTERED AT 10:10:29 ON 25 AUG 2006

L8 6985 SEA ABB=ON PLU=ON L7

FILE 'CAPLUS' ENTERED AT 10:13:55 ON 25 AUG 2006

D SCAN L1

FILE 'REGISTRY' ENTERED AT 10:14:57 ON 25 AUG 2006

FILE 'CAPLUS' ENTERED AT 10:15:00 ON 25 AUG 2006

L9 17230 SEA ABB=ON PLU=ON L4 (L) (PAC OR THU OR BAC OR PKT OR
DMA)/RL

FILE 'HCAPLUS' ENTERED AT 10:16:01 ON 25 AUG 2006

E HCV/CT
E E3+ALL
L10 12372 SEA ABB=ON PLU=ON (HCV+PFT/CT OR "CLASSICAL SWINE FEVER
VIRUS"+PFT/CT OR "HEPATITIS C VIRUS"+PFT/CT)
E HEPATITIS C/CT
E E5+ALL
L11 11667 SEA ABB=ON PLU=ON "HEPATITIS C VIRUS"+PFT/CT
L12 15162 SEA ABB=ON PLU=ON (HCV OR H(1A)C(1A)V OR HEPATITIS C
VIRUS?)/OBI,BI
L13 90130 SEA ABB=ON PLU=ON ((VIRAL?)/OBI,BI
L14 55395 SEA ABB=ON PLU=ON (ANTIVIRAL?)/OBI,BI
L15 4441 SEA ABB=ON PLU=ON L9 AND (L10 OR L11 OR L12 OR L13 OR L14)
L16 247 SEA ABB=ON PLU=ON L9 AND (L10 OR L11 OR L12)
L17 53 SEA ABB=ON PLU=ON L16 NOT (PY>2002 OR AY>2002 OR PRY>2002)

FILE 'REGISTRY' ENTERED AT 10:20:51 ON 25 AUG 2006

L18 STRUCTURE UPLOADED
L19 50 SEA SUB=L4 SSS SAM L18

FILE 'STNGUIDE' ENTERED AT 10:21:24 ON 25 AUG 2006

FILE 'REGISTRY' ENTERED AT 10:24:46 ON 25 AUG 2006

L20 STRUCTURE UPLOADED
L21 32 SEA SUB=L4 SSS SAM L20
L22 779 SEA SUB=L4 SSS FUL L20
SAVE L22 DEVESH875/A TEMP

FILE 'CAPLUS' ENTERED AT 10:25:44 ON 25 AUG 2006

L23 279 SEA ABB=ON PLU=ON L22 (L) (PAC OR THU OR BAC OR PKT OR
DMA)/RL

FILE 'HCAPLUS' ENTERED AT 10:26:29 ON 25 AUG 2006

L24 20 SEA ABB=ON PLU=ON L23 AND (L10 OR L11 OR L12)
L25 1 SEA ABB=ON PLU=ON L24 NOT (PY>2002 OR AY>2002 OR PRY>2002)

FILE 'STNGUIDE' ENTERED AT 10:27:09 ON 25 AUG 2006

FILE 'HCAPLUS' ENTERED AT 10:31:23 ON 25 AUG 2006

L26 177 SEA ABB=ON PLU=ON L23 NOT (PY>2002 OR AY>2002 OR PRY>2002)
L27 168 SEA ABB=ON PLU=ON L23 AND (L10 OR L11 OR L12 OR L13 OR L14)
L28 20 SEA ABB=ON PLU=ON L27 AND (L10 OR L11 OR L12)
L29 1 SEA ABB=ON PLU=ON L28 NOT (PY>2002 OR AY>2002 OR PRY>2002)

FILE 'REGISTRY' ENTERED AT 10:37:08 ON 25 AUG 2006

FILE 'HCAPLUS' ENTERED AT 10:37:58 ON 25 AUG 2006

D BIB L28 1
D BIB L26 1
L30 59 SEA ABB=ON PLU=ON L27 AND (HEPATITIS? OR HCV? OR H(1A)C(1A)V?
)
D BIB L30 1

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          D BIB L30 2
L31      170 SEA ABB=ON  PLU=ON  L23 NOT (PY>2001 OR AY>2001 OR PRY>2001)
          D BIB 1
L32      177 SEA ABB=ON  PLU=ON  (L26 OR L31)
L33      20  SEA ABB=ON  PLU=ON  L30 AND L24
L34      59  SEA ABB=ON  PLU=ON  (L30 OR L33)
L35      52  SEA ABB=ON  PLU=ON  L17 NOT L34
L36      51  SEA ABB=ON  PLU=ON  L35 AND (HEPATITIS? OR HCV? OR H(1A)C(1A)V?
          )
          E SCHINAZI R/AU
L37      511 SEA ABB=ON  PLU=ON  ("SCHINAZI R"/AU OR "SCHINAZI R F"/AU OR
          "SCHINAZI RAYMOND"/AU OR "SCHINAZI RAYMOND F"/AU OR "SCHINAZI
          RAYMOND FELIX"/AU OR "SCHINAZI REYMOND F"/AU)
          E STRIKER R/AU
L38      14  SEA ABB=ON  PLU=ON  ("STRIKER R"/AU OR "STRIKER ROBERT"/AU OR
          "STRIKER ROBERT T"/AU)
          E SHI J/AU
L39      6019 SEA ABB=ON  PLU=ON  SHI J?/AU
L40      30  SEA ABB=ON  PLU=ON  (L37 AND (L38 OR L39)) OR (L38 AND L39)
```

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FILE LAST UPDATED: 24 Aug 2006 (20060824/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que l40

L37 511 SEA FILE=HCAPLUS ABB=ON PLU=ON ("SCHINAZI R"/AU OR "SCHINAZI R F"/AU OR "SCHINAZI RAYMOND"/AU OR "SCHINAZI RAYMOND F"/AU OR "SCHINAZI RAYMOND FELIX"/AU OR "SCHINAZI REYMOND F"/AU)
L38 14 SEA FILE=HCAPLUS ABB=ON PLU=ON ("STRIKER R"/AU OR "STRIKER ROBERT"/AU OR "STRIKER ROBERT T"/AU)
L39 6019 SEA FILE=HCAPLUS ABB=ON PLU=ON SHI J?/AU
L40 30 SEA FILE=HCAPLUS ABB=ON PLU=ON (L37 AND (L38 OR L39)) OR (L38 AND L39)

=> d ibib abs l40 tot

L40 ANSWER 1 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:760529 HCAPLUS

TITLE: Modulation of 5-fluorouracil host-toxicity and chemotherapeutic efficacy against human colon tumors by 5-(Phenylthio)acyclouridine, a uridine phosphorylase inhibitor

AUTHOR(S): Al Safarjalani, Omar N.; Rais, Reem; *Shi, Junxing; Schinazi, Raymond F.*; Naguib, Fardos N. M.; el Kouni, Mahmoud H.

CORPORATE SOURCE: Department of Pharmacology and Toxicology, Comprehensive Cancer Center, Center for Aids Research, University of Alabama at Birmingham, Birmingham, AL, 35294, USA

SOURCE: Cancer Chemotherapy and Pharmacology (2006), 58(5), 692-698

CODEN: CCPHDZ; ISSN: 0344-5704

PUBLISHER: Springer

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Purpose: The purpose of this investigation was to evaluate the effectiveness of oral 5-(phenylthio)acyclouridine (PTAU) in reducing 5-fluorouracil (FUra) host-toxicity and enhancing its chemotherapeutic efficacy against human colon tumors. PTAU is a potent and specific inhibitor of uridine phosphorylase (UrdPase, EC 2.4.2.3), the enzyme responsible for uridine catabolism. Methods: SCID mice bearing human colon DLD-1 or HCT-15 tumors were injected i.p. with FUra (50, 200 or 300 mg/kg) on days 17, 24 and 31 after tumor cell inoculation. PTAU (120 mg/kg), uridine (1,320 mg/kg) or their combination was administered orally 2 or 4 h after FUra injection. Another four administrations of PTAU + uridine were given every 8 h after the first treatment with PTAU plus uridine. Survival and body weight were used to evaluate host toxicity. Tumor weight was used to evaluate the efficacy of the drugs on tumor growth. The mice were monitored for 38 days. Results: Administration of the maximum tolerated dose (50 mg/kg) of FUra reduced DLD-1 and HCT-15 tumor wts. by

48 and 59%, resp., at day 38 post implantation. Administration of 200 mg/kg FURA resulted in 100% mortality. Oral administration of uridine (1,320 mg/kg) alone, 2 h following the administration of 200 mg/kg FURA, did not alleviate FURA host-toxicity as all the mice died. Administration of 120 mg/kg PTAU resulted in partial rescue from this LD of FURA as 63% of mice survived and tumor wts. were reduced by approx. 60%. Coadministration of PTAU plus uridine resulted in complete rescue from the toxicity of FURA as 100% of the mice survived and tumor wts. were reduced by 81-82%. Delaying the administration of the combination of PTAU plus uridine to 4 h post FURA treatment was less effective in rescuing from FURA toxicity as only 88% of the mice survived and tumor wts. were reduced by only 62%. Administration of PTAU alone, under the same conditions, resulted in a 38% survival rate while the tumor wts. were reduced by 47%. Treatment with uridine alone did not protect from FURA toxicity at the dose of 200 mg/kg as all mice died. At the higher dose of 300 mg/kg FURA, neither uridine nor PTAU alone, administered 2 h following the treatment with FURA, had any rescuing effect. On the other hand, the use of the PTAU plus uridine combination reduced the tumor weight by 79%, although this reduction in the tumor weight was accompanied by 37% mortality. There was no significant difference between DLD-1 and HCT-15 in their response to the different regimens employed in this study despite the fact that the tumors have different levels of UrdPase. Conclusions: The present results demonstrate that the combination of PTAU plus uridine represents an exceptionally efficient method in increasing FURA chemotherapeutic efficacy while minimizing its host-toxicity. The efficiency of the PTAU plus uridine combination can be attributed to the extraordinary effectiveness of this combination in raising and maintaining higher levels of uridine in vivo (Al Safarjalani et al., Cancer Chemo Pharmacol 55:541-551, 2005). Therefore, the combination of PTAU plus uridine can provide a better substitute for the large doses of uridine necessary to rescue or protect from FURA host-toxicities, without the toxic side-effects associated with such doses of uridine. This combination may also allow for the escalation of FURA doses for better chemotherapeutic efficacy against human colon carcinoma while avoiding FURA host-toxicities. Alternatively, the combination of PTAU and uridine may be useful as an antidote in the few cases when cancer patients receive a lethal overdose of FURA.

L40 ANSWER 2 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1197406 HCAPLUS

TITLE: N4-hydroxycytosine dioxolane nucleosides and their activity against hepatitis B virus

AUTHOR(S): Du, Jinfa; Hollecker, Laurent; *Shi, Junxing*; Chun, Byoung-Kwon; Watanabe, Kyoichi A.; *Schinazi, Raymond F.*; Nachman, Tammy Y.; Lostia, Stefania; Stuyver, Lieven J.; Otto, Michael J.

CORPORATE SOURCE: Pharmasset, Inc., Tucker, GA, USA

SOURCE: Nucleosides, Nucleotides & Nucleic Acids (2005), 24(8), 1209-1214

CODEN: NNNAFY; ISSN: 1525-7770

PUBLISHER: Taylor & Francis, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Novel racemic, D- and L- β -dioxolane N4-hydroxycytosine nucleosides have been synthesized and evaluated for their activity against hepatitis B virus. None of the synthesized nucleosides demonstrated selective anti-HBV activity.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 3 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1151410 HCAPLUS
TITLE: Synthesis and in vitro anti-HCV activity of β -D- and L-2'-deoxy-2'-fluororibonucleosides
AUTHOR(S): **Shi, Junxing**; Du, Jinfa; Ma, Tianwei; Pankiewicz, Krzysztof W.; Patterson, Steven E.; Hassan, Abdalla E. A.; Tharnish, Phillip M.; McBrayer, Tamara R.; Lostia, Stefania; Stuyver, Lieven J.; Watanabe, Kyoichi A.; Chu, Chung K.; **Schinazi, Raymond F.**
CORPORATE SOURCE: Pharmasset, Inc., Tucker, GA, USA
SOURCE: Nucleosides, Nucleotides & Nucleic Acids (2005), 24(5-7), 875-879
CODEN: NNNAFY; ISSN: 1525-7770
PUBLISHER: Taylor & Francis, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Based on the discovery of β -D-2'-deoxy-2'-fluorocytidine as a potent anti-hepatitis C virus (HCV) agent, a series of β -D- and L-2'-deoxy-2'-fluororibonucleosides with modifications at 5 and/or 4 positions were synthesized and evaluated for their in vitro activity against HCV and bovine viral diarrhea virus (BVDV). The introduction of the 2'-fluoro group was achieved by either fluorination of 2,2'-anhydronucleosides with hydrogen fluoride-pyridine or potassium fluoride, or a fluorination of arabinonucleosides with DAST. Among the 27 analogs synthesized, only the 5-fluoro compds., namely β -D-2'-deoxy-2',5-difluorocytidine (5), had anti-HCV activity in the subgenomic HCV replicon cell line, and inhibitory activity against rRNA. As β -D-N4-hydroxycytidine (NHC) had previously shown potent anti-HCV activity, the two functionalities of the N4-hydroxyl and the 2'-fluoro were combined into one mol., yielding β -D-2'-deoxy-2'-fluoro-N4-hydroxycytidine (12). However, this nucleoside showed neither anti-HCV activity nor toxicity. All the L-forms of the analogs were devoid of anti-HCV activity. None of the compds. showed anti-BVDV activity, suggesting that the BVDV system cannot reliably predict anti-HCV activity in vitro.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 4 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:619606 HCAPLUS
DOCUMENT NUMBER: 143:298527
TITLE: Characterization of hepatitis B virus inhibition by novel 2'-fluoro-2',3'-unsaturated beta-D- and L-nucleosides
AUTHOR(S): Pai, S. Balakrishna; Pai, Rekha B.; Xie, Meng-yu; Beker, Tolunay; **Shi, Junxing**; Tharnish, Philip M.; Chu, Chung K.; **Schinazi, Raymond F.**
CORPORATE SOURCE: Veterans Affairs Medical Center, Decatur, GA, USA
SOURCE: Antiviral Chemistry & Chemotherapy (2005), 16(3), 183-192
CODEN: ACCHEH; ISSN: 0956-3202
PUBLISHER: International Medical Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The clin. emergence of lamivudine and adefovir resistance mutations on prolonged therapy further necessitates the development of addnl. drugs for the treatment of hepatitis B virus (HBV) infections. The authors have

evaluated a number of novel 2'-fluoro-2',3'-unsatd. D- and L-nucleosides for their anti-HBV activity in the HepG2-2.2.15 cell system. The most potent nucleosides were β -L-2'-fluoro-2',3'-dideoxy-2',3'-didehydrocytidine (L-2'-Fd4C) and β -L-2'-fluoro-2',3'-dideoxy-2',3'-didehydro-5-fluorocytidine (L-2'-Fd4FC) with median effective concns. (EC₅₀) of 0.002 μ M and 0.004 μ M, resp. The D-enantiomers of the 2'-fluoro-substituted cytidine analogs in this series showed activity, with the 5-fluorocytidine (D-2'-Fd4FC) being the most potent (EC₅₀=0.05 μ M). The active compds. were not cytotoxic to a number of cell lines or to bone marrow progenitor cells. Furthermore, mitochondrial DNA synthesis and function were not affected by these nucleosides. L-2'-Fd4C did not affect viral transcription, implying that it does not inhibit cellular RNA polymerase II. Studies with the HBV polymerase in core particles revealed that the 5'-triphosphates of L-2'-Fd4C and D-2'-Fd4FC produced a dose-dependent inhibition of the incorporation of 32P-dCTP into the HBV DNA, indicating that the mechanism of action of these compds. is through specific inhibition of viral DNA synthesis. This class of nucleosides, which exhibit potent antiviral activity and a favorable safety profile, have potential for the treatment of HBV infections and warrant further development.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 5 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:377558 HCAPLUS

DOCUMENT NUMBER: 143:125779

TITLE: 5-(Phenylthio)acyclouridine: a powerful enhancer of oral uridine bioavailability: relevance to chemotherapy with 5-fluorouracil and other uridine rescue regimens

AUTHOR(S): Al Safarjalani, Omar N.; Zhou, Xiao-Jian; Rais, Reem H.; *Shi, Junxing; Schinazi, Raymond F.*; Naguib, Fardos N. M.; el Kouni, Mahmoud H.

CORPORATE SOURCE: Department of Pharmacology and Toxicology, Comprehensive Cancer Center, Center for AIDS Research, University of Alabama at Birmingham, Birmingham, AL, 35294, USA

SOURCE: Cancer Chemotherapy and Pharmacology (2005), 55(6), 541-551

CODEN: CCPHDZ; ISSN: 0344-5704

PUBLISHER: Springer GmbH

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The purpose of this investigation was to evaluate the effectiveness of oral 5-(phenylthio)acyclouridine (PTAU) in improving the pharmacokinetics and bioavailability of oral uridine. PTAU is a potent and specific inhibitor of uridine phosphorylase (UrdPase, EC 2.4.2.3), the enzyme responsible for uridine catabolism. This compound was designed as a lipophilic inhibitor in order to facilitate its access to the liver and intestine, the main organs involved in uridine catabolism. PTAU is fully absorbed after oral administration with 100% oral bioavailability. Uridine (330, 660 or 1320 mg/kg) and/or PTAU (30, 45, 60, 120, 240 or 480 mg/kg) were orally administered to mice. The plasma levels of uridine, its catabolite uracil, and PTAU were measured using HPLC, and pharmacokinetic anal. was performed. Oral PTAU up to 480 mg/kg per day is not toxic to mice. Oral PTAU at 30, 45, 60, 120 and 240 mg/kg has a prolonged plasma half-life of 2-3 h, and peak plasma PTAU concns. (C_{max}) of 41, 51, 74, 126 and 161 μ M with AUCs of 70, 99, 122, 173 and 225 μ mol h/l, resp. Coadministration of uridine with PTAU did not have a

significant effect on the pharmacokinetic parameters of plasma PTAU at any of the doses tested. Coadministration of PTAU (30, 45, 60 and 120 or 240 mg/kg) with uridine (330, 660 or 1320 mg/kg) elevated the concentration of plasma

uridine over that following the same dose of uridine alone, a result of reduced metabolic clearance of uridine as evidenced by decreased plasma exposure (Cmax and AUC) to uracil. Plasma uridine was elevated with the increase of uridine dose at each PTAU dose tested and no plateau was reached. Coadministration of PTAU at 30, 45, 60, 120 and 240 mg/kg improved the low oral bioavailability (7.7%) of uridine administered at 1320 mg/kg by 4.3-, 5.9-, 9.9-, 11.7- and 12.5-fold, resp., and reduced the AUC of plasma uracil (1227.8 $\mu\text{mol h/l}$) by 5.7-, 6.8-, 8.2-, 6.3-, and 6.9-fold, resp. Similar results were observed when PTAU was coadministered with lower doses of uridine. Oral PTAU at 30, 45, 60, 120 and 240 mg/kg improved the oral bioavailability of 330 mg/kg uridine by 1.7-, 2.4-, 2.6-, 5.2- and 4.3- fold, and that of 660 mg/kg uridine by 2.3-, 2.7-, 3.3-, 4.6- and 6.7-fold, resp. The excellent pharmacokinetic properties of PTAU, and its extraordinary effectiveness in improving the oral bioavailability of uridine, could be useful to rescue or protect from host toxicities of 5-fluorouracil and various chemotherapeutic pyrimidine analogs used in the treatment of cancer and AIDS, as well as in the management of medical disorders that are remedied by the administration of uridine including CNS disorders (e.g. Huntington's disease, bipolar disorder), liver diseases, diabetic neuropathy, cardiac damage, various autoimmune diseases, and transplant rejection.

REFERENCE COUNT: 89 THERE ARE 89 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 6 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:105999 HCAPLUS

DOCUMENT NUMBER: 142:374059

TITLE: Synthesis and anti-viral activity of a series of D- and L-2'-deoxy-2'-fluororibonucleosides in the subgenomic HCV replicon system

AUTHOR(S): **Shi, Junxing**; Du, Jinfa; Ma, Tianwei; Pankiewicz, Krzysztof W.; Patterson, Steven E.; Tharnish, Phillip M.; McBrayer, Tamara R.; Stuyver, Lieven J.; Otto, Michael J.; Chu, Chung K.; **Schinazi, Raymond F.**; Watanabe, Kyoichi A.

CORPORATE SOURCE: Pharmasset, Inc., Tucker, GA, 30084, USA

SOURCE: Bioorganic & Medicinal Chemistry (2005), 13(5), 1641-1652

CODEN: BMECEP; ISSN: 0968-0896

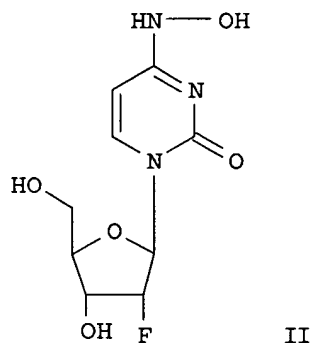
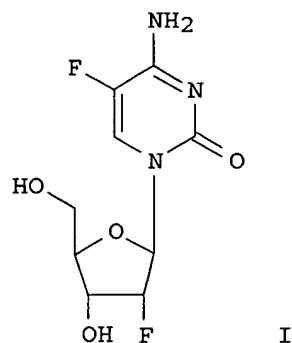
PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 142:374059

GI



AB Based on the discovery of (2'R)--2'-deoxy-2'-fluorocytidine as a potent anti-hepatitis C virus (HCV) agent, a series of D- and L-2'-deoxy-2'-fluororibonucleosides with modifications at 5- and/or 4-positions were synthesized and evaluated for their in vitro activity against HCV and bovine viral diarrhea virus (BVDV). The key step in the synthesis, the introduction of 2'-fluoro group, was achieved by either fluorination of 2,2'-anhydronucleosides with hydrogen fluoride-pyridine or potassium fluoride, or a fluorination of arabinonucleosides with DAST. Among the 27 analogs synthesized, only the 5-fluoro compound, namely (2'R)-D-2'-deoxy-2',5-difluorocytidine (I), demonstrated potent anti-HCV activity and toxicity to rRNA. The replacement of the 4-amino group with a thiol group resulted in the loss of activity, while the 4-methylthio substituted analog exhibited inhibition of rRNA. As N4-hydroxycytidine (NHC) had previously shown potent anti-HCV activity, we combined the two functionalities of the N4-hydroxyl and the 2'-fluoro into one mol., resulting (2'R)-D-2'-deoxy-2'-fluoro-N4-hydroxycytidine (II). However, this nucleoside showed neither anti-HCV activity nor toxicity. All the L-forms of the analogs were devoid of anti-HCV activity. None of the compds. showed anti-BVDV activity, suggesting that the BVDV system cannot always predict anti-HCV activity.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 7 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:416113 HCAPLUS

DOCUMENT NUMBER: 141:350352

TITLE: Synthesis of β -enantiomers of N4-hydroxy-3'-deoxypyrimidine nucleosides and their evaluation against bovine viral diarrhoea virus and hepatitis C virus in cell culture

AUTHOR(S): Hollecker, Laurent; Choo, Hyunah; Chong, Youhoon; Chu, Chung K.; Lostia, Stefania; McBrayer, Tamara R.; Stuyver, Lieven J.; Mason, J. Christian; Du, Jinfa; Rachakonda, Suguna; **Shi, Junxing**; **Schinazi, Raymond F.**; Watanabe, Kyochi A.

CORPORATE SOURCE: Pharmasset Inc., Tucker, GA, USA

SOURCE: Antiviral Chemistry & Chemotherapy (2004), 15(1), 43-55

CODEN: ACCHEH; ISSN: 0956-3202

PUBLISHER: International Medical Press

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 141:350352

AB N4-Hydroxycytidine (NHC) was recently reported to have anti-pestivirus and

anti-hepacivirus activity. It is thought that this nucleoside acts as a weak alternative substrate for the hepatitis C virus (HCV) polymerase. In addition to NHC, 3'-deoxyuridine (3'-dU) was found to inhibit bovine diarrhoea virus (BVDV) production by 1 log₁₀ at 37.2 µM. These initial findings prompted the synthesis of β-D and β-L analogs of (i) base-modified 3'-deoxy-NHC; (ii) 3'-deoxyuridine; and 3'-deoxycytidine. The antiviral activity of these 42 nucleosides was evaluated against BVDV and HCV bicistronic replicon in cell culture. Among the NHC analogs, the antiviral activity observed for the β-L-3'-deoxy-5-fluoro-derivative 1-(3-deoxy-β-L-erythro-pentofuranosyl)-5-fluoro-4-hydroxyaminopyrimidin-2(1H)-one and the β-D-3'-deoxy-5-iodo-derivative 1-(3-deoxy-β-D-erythro-pentofuranosyl)-5-iodocytosine in the replicon system (1 log₁₀ reduction at 100 µM) was due to the concomitant toxicity towards intracellular rRNA levels (CC₉₀ equal or lower than the EC₉₀). In conclusion, none of the newly synthesized derivs. exhibited enhanced antiviral activity compared to the parent nucleoside NHC.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 8 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:303282 HCAPLUS

DOCUMENT NUMBER: 141:54565

TITLE: 2',3'-Didehydro-2',3'-dideoxynucleosides are degraded to furfuryl alcohol under acidic conditions

AUTHOR(S): **Shi, Junxing**; Ray, Adrian S.; Mathew, Judy S.; Anderson, Karen S.; Chu, Chung K.; **Schinazi, Raymond F.**

CORPORATE SOURCE: Department of Pediatrics, Emory University School of Medicine, Atlanta, GA, 30323, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(9), 2159-2162

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 141:54565

AB 2',3'-Didehydro-2',3'-dideoxynucleosides are clin. relevant antiviral agents. These nucleosides could be degraded under acidic conditions. Acidic stability studies showed the D4N had the following increasing stability order: D4G < cyclo-D4G ≤ RVT < D4T with half-lives ranging from less than 2 min to 35 days. A concerted A-1 mechanism has been proposed for the acidic cleavage of D4-nucleosides. The cleavage products were characterized as furfuryl alc. and the corresponding nucleobase. Furfuryl alc. is an agent found in many everyday food products. The biol. results demonstrated that furfuryl alc. had neither anti-HIV activity nor cytotoxicity in vitro, suggesting the acid instability of D4-nucleosides is unlikely to have an impact on the toxicity of these nucleoside analogs in humans.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 9 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:120958 HCAPLUS

DOCUMENT NUMBER: 140:157421

TITLE: 2',3'-dideoxynucleoside analogs for the treatment or prevention of flaviviridae infections

INVENTOR(S): **Shi, Junxing**; **Schinazi, Raymond F.**; **Striker, Robert**

PATENT ASSIGNEE(S): Pharmasset Ltd., Barbados; Emory University; Board of

SOURCE: Trustees of the Leland Stanford Junior University
PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004013298	A2	20040212	WO 2003-US24288	20030801
WO 2004013298	A3	20040401		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2003263978	A1	20040223	AU 2003-263978	20030801
US 2004067877	A1	20040408	US 2003-632875	20030801
PRIORITY APPLN. INFO.:			US 2002-453715P	P 20020801
			US 2002-453716P	P 20020801
			WO 2003-US24288	W 20030801

OTHER SOURCE(S): MARPAT 140:157421

AB A method for the treatment or prevention of flaviviridae infections, in particular, hepatitis C virus infection, in a host, and in particular, a human, is provided that includes administering an effective amount of a 2',3'-dideoxynucleoside or a pharmaceutically acceptable salt or prodrug thereof, optionally in a pharmaceutically acceptable diluent or excipient. Preparation of compds. of the invention is included.

L40 ANSWER 10 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:115659 HCAPLUS

DOCUMENT NUMBER: 140:263853

TITLE: Inhibition of the subgenomic hepatitis C virus replicon in Huh-7 cells by 2'-deoxy-2'-fluorocytidine
AUTHOR(S): Stuyver, Lieven J.; McBrayer, Tamara R.; Whitaker, Tony; Tharnish, Phillip M.; Ramesh, Mangala; Lostia, Stefania; Cartee, Leanne; **Shi, Junxing**; Hobbs, Ann; **Schinazi, Raymond F.**; Watanabe, Kyoichi A.; Otto, Michael J.

CORPORATE SOURCE: Pharmasset, Inc., Tucker, GA, 30084, USA

SOURCE: Antimicrobial Agents and Chemotherapy (2004), 48(2), 651-654

CODEN: AMACQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 2'-Deoxy-2'-fluorocytidine (FdC) is a potent inhibitor of the hepatitis C virus RNA replicon in culture, and FdC-5'-triphosphate is an effective inhibitor of the NS5B polymerase. Dynamic profiling of cell growth in an antiviral assay showed that FdC caused cytostasis due to an S-phase arrest. These observations demonstrate that FdC treatment is affecting both a viral target and a cellular target.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 11 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:752167 HCAPLUS

DOCUMENT NUMBER: 140:121863

TITLE: Probing the mechanistic consequences of 5-fluorine substitution on cytidine nucleotide analogue incorporation by HIV-1 reverse transcriptase

AUTHOR(S): Ray, Adrian S.; *Schinazi, Raymond F.*; Murakami, Eisuke; Basavapathruni, Aravind; *Shi, Junxing*; Zorca, Suzana M.; Chu, Chung K.; Anderson, Karen S.

CORPORATE SOURCE: Department of Pharmacology, Yale University School of Medicine, New Haven, CT, USA

SOURCE: Antiviral Chemistry & Chemotherapy (2003), 14(3), 115-125

CODEN: ACCHEH; ISSN: 0956-3202

PUBLISHER: International Medical Press

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with refs. β -D and β -L-enantiomers of 2',3'-dideoxycytidine analogs are potent chain-terminators and antimetabolites for viral and cellular replication. Seemingly small modifications markedly alter their antiviral and toxicity patterns. This review discusses previously published and recently obtained data on the effects of 5- and 2'-fluorine substitution on the pre-steady state incorporation of 2'-deoxycytidine-5'-monophosphate analogs by HIV-1 reverse transcriptase (RT) in light of their biol. activity. The addition of fluorine at the 5-position of the pyrimidine ring altered the kinetic parameters for all nucleotides tested. Only the 5-fluorine substitution of the clin. relevant nucleosides (-)- β -L-2',3'-dideoxy-3'-thia-5-fluorocytidine (L-FTC, Emtriva), and (+)- β -D-2',3'-didehydro-2',3'-dideoxy-5-fluorocytidine (D-D4FC, Reverset), caused a higher overall efficiency of nucleotide incorporation during both DNA- and RNA-directed synthesis. Enhanced incorporation by RT may in part explain the potency of these nucleosides against HIV-1. In other cases, a lack of correlation between RT incorporation in enzymic assays and antiviral activity in cell culture illustrates the importance of other cellular factors in defining antiviral potency. The substitution of fluorine at the 2' position of the deoxyribose ring neg. affects incorporation by RT indicating the steric gate of RT can detect electrostatic perturbations. Intriguing results pertaining to drug resistance have led to a better understanding of HIV-1 RT resistance mechanisms. These insights serve as a basis for understanding the mechanism of action for nucleoside analogs and, coupled with studies on other key enzymes, may lead to the more effective use of fluorine to enhance the potency and selectivity of antiviral agents.

REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 12 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:661457 HCAPLUS

DOCUMENT NUMBER: 140:192186

TITLE: N4-acyl-modified D-2',3'-dideoxy-5-fluorocytidine nucleoside analogues with improved antiviral activity

AUTHOR(S): *Shi, Junxing*; Mathew, Judy S.; Tharnish, Phillip M.; Rachakonda, Suguna; Pai, S. Balakrishna; Adams, Marjorie; Grier, Jason P.; Gallagher, Karen; Zhang, Hangchun; Wu, Jing-Tao; Shi, Guoen; Geleziunas, Romas; Erickson-Viitanen, Susan; Stuyver, Lieven;

OTTO, Michael J.; Watanabe, Kyoichi A.; **Schinazi, Raymond F.**
CORPORATE SOURCE: Pharmasset, Inc., Tucker, GA, USA
SOURCE: Antiviral Chemistry & Chemotherapy (2003), 14(2), 81-90
CODEN: ACCHEH; ISSN: 0956-3202
PUBLISHER: International Medical Press
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:192186

AB A series of 2',3'-dideoxy (D2) and 2',3'-didehydro-2',3'-dideoxy (D4) 5-fluorocytosine nucleosides modified with substituted benzoyl, heteroarom. carbonyl, cycloalkylcarbonyl and alkanoyl at the N4-position were synthesized and evaluated for anti-human immunodeficiency virus type 1 (HIV-1) and anti-hepatitis B virus (HBV) activity in vitro. For most D2-nucleosides, N4-substitutions improved the anti-HIV-1 activity markedly without increasing the cytotoxicity. In the D4-nucleosides series, some of the substituents at the N4-position enhanced the anti-HIV-1 activity with a modest increase in the cytotoxicity. The most potent and selective N4-modified nucleoside for the D2-series was N4-p-iodobenzoyl-D2FC, which had a 46-fold increase in anti-HIV-1 potency in MT-2 cells compared to the parent nucleoside D-D2FC. In the D4-series, N4-p-bromobenzoyl-D4FC was 12-fold more potent in MT-2 cells compared to the parent nucleoside D-D4FC. All eight N4-p-halobenzoyl-substituted D2- and D4-nucleosides evaluated against HBV in HepAD38 cells demonstrated equal or greater potency than the two parental compds., D-D2FC and D-D4FC. The N4-modification especially in the D2-nucleoside series containing the N4-nicotinoyl, o-nitrobenzoyl and n-butyryl showed a significant reduction in mitochondrial toxicity relative to the parent nucleoside analog. Although the 5'-triphosphate of the parent compound (D-D4FC-TP) was formed from the N4-acyl-D4FC analogs in different cells, the levels of the 5'-triphosphate nucleotide did not correlate with the cell-derived 90% effective antiviral concns. (EC90), suggesting that a direct interaction of the triphosphates of these N4-acyl nucleosides was involved in the antiviral activity.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 13 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:511093 HCAPLUS
DOCUMENT NUMBER: 139:79113
TITLE: Treatment of EBV and KHSV infection and associated abnormal cellular proliferation
INVENTOR(S): **Schinazi, Raymond F.; Shi, Junxing**
; Fingerroth, Joyce D.; Gustafson, Erik
PATENT ASSIGNEE(S): Pharmasset Ltd., Barbados; Beth Israel Deaconess Medical Center; Emory University
SOURCE: PCT Int. Appl., 138 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003053360	A2	20030703	WO 2002-US40853	20021219
WO 2003053360	A3	20050707		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
CA 2470938 AA 20030703 CA 2002-2470938 20021219
AU 2002360697 A1 20030709 AU 2002-360697 20021219
US 2003176392 A1 20030918 US 2002-326444 20021219
EP 1569658 A2 20050907 EP 2002-795977 20021219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, FI, CY, TR, BG, CZ, EE, SK
JP 2005528334 T2 20050922 JP 2003-554120 20021219
PRIORITY APPLN. INFO.: US 2001-345130P P 20011220
WO 2002-US40853 W 20021219

OTHER SOURCE(S): MARPAT 139:79113

AB A method and composition for the treatment, prevention and/or prophylaxis of a host, and in particular, a human, infected with Epstein-Barr virus (EBV), is provided that includes administering an effective amount of a 5-substituted uracil nucleoside or its pharmaceutically acceptable salt or prodrug, optionally in a pharmaceutically acceptable diluent or excipient.

L40 ANSWER 14 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:26945 HCAPLUS

DOCUMENT NUMBER: 139:381

TITLE: Ribonucleoside analogue that blocks replication of bovine viral diarrhea and hepatitis C viruses in culture

AUTHOR(S): Stuyver, Lieven J.; Whitaker, Tony; McBrayer, Tamara R.; Hernandez-Santiago, Brenda I.; Lostia, Stefania; Tharnish, Phillip M.; Ramesh, Mangala; Chu, Chung K.; Jordan, Robert; *Shi, Junxing*; Rachakonda, Suguna; Watanabe, Kyoichi A.; Otto, Michael J.; *Schinazi, Raymond F.*

CORPORATE SOURCE: Pharmasset Inc., Tucker, GA, 30084, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2003), 47(1), 244-254

CODEN: AMACQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A base-modified nucleoside analog, β -D-N4-hydroxycytidine (NHC), was found to have antipestivirus and antihepacivirus activities. This compound inhibited the production of cytopathic bovine viral diarrhea virus (BVDV) RNA in a dose-dependent manner with a 90% effective concentration (EC90) of 5.4 μ M, an observation that was confirmed by virus yield assays (EC90 = 2 μ M). When tested for hepatitis C virus (HCV) replicon RNA reduction in Huh7 cells, NHC had an EC90 of 5 μ M on day 4. The HCV RNA reduction was incubation time and nucleoside concentration dependent. The in vitro antiviral effect of NHC was additive with recombinant alpha interferon-2a and could be prevented by the addition of exogenous cytidine and uridine but not of other natural ribo- or 2'-deoxynucleosides. When HCV RNA replicon cells were cultured in the presence of increasing concns. of NHC (up to 40 μ M) for up to 45 cell passages, no resistant replicon was selected. Similarly, resistant BVDV could not be selected after 20 passages. NHC was phosphorylated to the triphosphate form in Huh7 cells, but in

cell-free HCV NS5B assays, synthetic NHC-triphosphate (NHC-TP) did not inhibit the polymerization reaction. Instead, NHC-TP appeared to serve as a weak

alternative substrate for the viral polymerase, thereby changing the mobility of the product in polyacrylamide electrophoresis gels. We speculate that incorporated nucleoside analogs with the capacity of changing the thermodyn. of regulatory secondary structures (with or without introducing mutations) may represent an important class of new antiviral agents for the treatment of RNA virus infections, especially HCV.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 15 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:5729 HCAPLUS

DOCUMENT NUMBER: 138:56191

TITLE: Preparation, antiviral activity, and cytotoxicity of β -2'- and 3'-halo-nucleosides

INVENTOR(S): Chu, Chung K.; Otto, Michael J.; **Shi, Junxing**; **Schinazi, Raymond F.**; Choi, Yongseok; Gumina, Giuseppe; Chong, Youhoon; et al.

PATENT ASSIGNEE(S): Pharmasset Ltd., Barbados; University of Georgia Research Foundation, Inc.; Emory University

SOURCE: PCT Int. Appl., 220 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

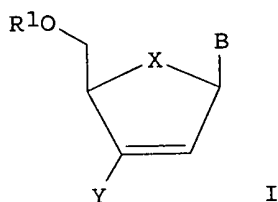
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000200	A2	20030103	WO 2002-US20245	20020624
WO 2003000200	A3	20040902		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2451745	AA	20030103	CA 2002-2451745	20020624
EP 1478322	A2	20041124	EP 2002-756310	20020624
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR			
JP 2005503358	T2	20050203	JP 2003-506646	20020624
CN 1599744	A	20050323	CN 2002-816455	20020624
US 2005119886	A1	20050602	US 2002-179612	20020624
US 6949522	B2	20050927		
BR 2002010594	A	20051101	BR 2002-10594	20020624
PRIORITY APPLN. INFO.:			US 2001-300356P	P 20010622
			US 2001-305386P	P 20010713
			WO 2002-US20245	W 20020624

OTHER SOURCE(S): MARPAT 138:56191

GI



AB The present invention includes compds. and compns. of β -halo-nucleosides I wherein: R1 is hydrogen, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, CO-aryloxyalkyl, CO-substituted aryl, alkylsulfonyl, arylsulfonyl, aralkylsulfonyl, amino acid residue, mono, di, or triphosphate, or a phosphate derivative; X is O, S, SO₂ or CH₂; Y is fluoro, chloro, bromo or iodo; and B is a purine or pyrimidine base that may optionally be substituted, as well as methods to treat HIV, HBV or abnormal cellular proliferation comprising administering said compds. or compns. Thus, (-)-1-[(1S,4R)-2,3-dideoxy-2,3-didehydro-2-fluoro-4-thio- β -D-ribofuranosyl]-cytosine was prepared and tested in vitro as antiviral agent. Preferred examples of antiviral agents can be used in combination or alternation with other known antiviral agents for HIV therapy. Use of the any one of the pharmaceutical compns. for the treatment and/or prophylaxis of an HIV infection or an abnormal cellular proliferation in a host.

L40 ANSWER 16 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:822154 HCAPLUS

DOCUMENT NUMBER: 138:395461

TITLE: Interactions of enantiomers of 2',3'-didehydro-2',3'-dideoxy-fluorocytidine with wild type and M184V mutant HIV-1 reverse transcriptase

AUTHOR(S): Ray, Adrian S.; Murakami, Eisuke; Peterson, Celeste N.; Shi, Junxing; Schinazi, Raymond F.; Anderson, Karen S.

CORPORATE SOURCE: Department of Pharmacology, Yale University School of Medicine, New Haven, CT, 06520-8066, USA

SOURCE: Antiviral Research (2002), 56(3), 189-205
CODEN: ARSRDR; ISSN: 0166-3542

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Both the β -D-(+) and β -L-(-)-enantiomers of 2',3'-didehydro-2',3'-dideoxy-5-fluorocytidine (D4FC) are clin. relevant compds. because of their potent anti-HIV and anti-HBV activities. Cross-resistance to 1-D4FC with HBV containing a mutation in the conserved polymerase YMDD region has been observed. In order to better understand the effects of stereochem. on planar 5-fluorinated cytidine analogs and to gain insight into resistance caused by YMDD mutations in HIV-1 reverse transcriptase (RT), a combination of transient kinetic studies and computer modeling were employed. In contrast to studies with the (+) and (-) isomers of 3TC-TP and FTC-TP, it was found that wild type RT had a high enantiomeric selectivity between the d-(+) and l-(-) isomers of D4FC-TP. While no resistance was conferred by the methionine 184 to valine mutation to d-D4FC-TP, l-D4FC-TP was incorporated 50- to 70-fold less efficiently. The kinetic parameters of incorporation in the presence of l-D4FC-TP by RTWT and the mechanism of resistance by RTM184V were found to be distinct from those seen with the corresponding l-isomers containing an oxathiolane ring: (-)-3TC-TP and (-)-FTC-TP. Mol. modeling suggests that l- and

d-D4FC-TP are positioned in the active site favorably for incorporation by RTWT and that l-D4FC-TP, but not d-D4FC-TP, is sterically hindered by the addition of a β branched amino acid at position 184 of RTM184V.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 17 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:310733 HCAPLUS

DOCUMENT NUMBER: 138:52001

TITLE: Preclinical development of β -D-5-o-carboranyl-2'-deoxyuridine for the treatment of malignant brain tumors

AUTHOR(S): **Schinazi, Raymond F.**; Hurwitz, Selwyn J.; Liberman, Irina; Juodawlkis, Amy; **Shi, Junxing**; Liotta, Dennis C.; Coderre, Jeffrey; Olson, Jeffrey

CORPORATE SOURCE: Emory University, Atlanta, GA, 30033, USA
SOURCE: Frontiers in Neutron Capture Therapy, [Proceedings of the International Symposium on Neutron Capture Therapy for Cancer], 8th, Los Angeles, CA, United States, Sept. 13-18, 1998 (2001), Meeting Date 1998, Volume 2, 1121-1124. Editor(s): Hawthorne, M. Frederick; Shelly, Kenneth; Wiersema, Richard J. Kluwer Academic/Plenum Publishers: New York, N. Y.
CODEN: 69CMQV; ISBN: 0-306-46442-X

DOCUMENT TYPE: Conference

LANGUAGE: English

AB The efficacy of boron neutron capture therapy (BNCT) with β -D-5-o-carboranyl-2'-deoxyuridine (D-CDU) for treating malignant brain tumors was evaluated using rats bearing intracranial 9L glioma cell tumors. The rats were divided into four groups, group 1 was untreated, groups 2 received neutron irradiation only and groups 3 and 4 received a single i.p. dose of 30 mg/kg and 150 mg/kg of D-CDU, resp., 2 h before neutron therapy. Group 1 rats had a median survival of 20 days and none survived longer than 27 days, while group 2 rats survived considerably longer than group 1 rats with a median survival of 32 days. Group 3 rats survived considerably longer than groups 2 rats, and the delay mortality for the group 4 rats was insignificantly greater than group 2 rats, which is related to the lower selectivity of C-DCU at the highest dose, based on the tumor/brain and brain/blood ratios. These results suggested an optimal dose could exist for D-CDU between 30 and 150 mg/kg for 20% enriched D-CDU.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 18 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:229532 HCAPLUS

DOCUMENT NUMBER: 136:395329

TITLE: Insights into the Molecular Mechanism of Inhibition and Drug Resistance for HIV-1 RT with Carbovir Triphosphate

AUTHOR(S): Ray, Adrian S.; Yang, Zhenjun; **Shi, Junxing**; Hobbs, Ann; **Schinazi, Raymond F.**; Chu, Chung K.; Anderson, Karen S.

CORPORATE SOURCE: Department of Pharmacology, Yale University School of Medicine, New Haven, CT, 06520-8066, USA

SOURCE: Biochemistry (2002), 41(16), 5150-5162

CODEN: BICHAW; ISSN: 0006-2960

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Abacavir (1592U89, or Ziagen) is a powerful and selective inhibitor of HIV-1 viral replication that has been approved by the FDA for treatment of acquired immunodeficiency syndrome. Abacavir is metabolized to the active compound carbovir triphosphate (CBVTP). This compound is a guanosine analog containing a 2',3'-unsatn. in its planar carbocyclic deoxyribose ring that acts on HIV-1 reverse transcriptase (RTWT) as a mol. target, resulting in chain termination of DNA synthesis. A single amino acid change from methionine 184 to valine in HIV-1 RT (RTM184V) has been observed clin. in response to abacavir treatment. The ability of the natural substrate, dGTP, or CBVTP to be utilized during DNA- and RNA-directed polymerization by

RTWT and RTM184V was defined by pre-steady-state kinetic parameters. In the case of RTWT, CBVTP was found to be a surprisingly poor substrate relative to dGTP. In both DNA- and RNA-directed polymerization, a decrease in the efficiency of CBVTP utilization with respect to dGTP was found with RTM184V, suggesting that this mutation confers resistance at the level of CBVTP incorporation. The relatively low incorporation efficiency for RTWT was unanticipated considering earlier studies showing that the triphosphate form of a thymidine nucleoside analog containing a planar 2',3'-unsatd. ribose ring, D4TTP, was incorporated with high efficiency relative to the natural substrate, dTTP. The difference may be related to the isosteric replacement of oxygen in the deoxyribose ring with carbon. This hypothesis was tested by synthesizing and evaluating D4GTP (the planar 2',3'-unsatd. deoxyribose guanosine analog that is complementary to D4TTP). In contrast to CBVTP, D4GTP was found to be an excellent substrate for RTWT and no resistance was conferred by the M184V mutation, thus providing novel insight into structure-activity relationships for nucleoside-based inhibitors. In this work, we illustrate how an understanding of the mol. mechanism of inhibition and drug resistance led to the discovery of a novel prodrug of D4G. This compound shows promise as a potent antiviral especially with the drug resistant M184V HIV-1 RT that is so often encountered in a clin. setting.

REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 19 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:797627 HCAPLUS

DOCUMENT NUMBER: 137:103407

TITLE: Enhancement of the bioavailability of oral uridine by

coadministration of 5-(phenylthio)acyclouridine, a uridine phosphorylase inhibitor: implications for uridine rescue regimens in chemotherapy

AUTHOR(S): Al Safarjalani, Omar N.; Zhou, Xiao-Jian; Naguib, Fardos N. M.; **Shi, Junxing; Schinazi, Raymond F.**; el Kouni, Mahmoud H.

CORPORATE SOURCE: Department of Pharmacology and Toxicology, University of Alabama at Birmingham, Center for AIDS Research, Comprehensive Cancer Center, Birmingham, AL, 35294, USA

SOURCE: Cancer Chemotherapy and Pharmacology (2001), 48(5), 389-397

CODEN: CCPHDZ; ISSN: 0344-5704

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The purpose of this investigation was to evaluate the effectiveness of oral 5-(phenylthio)acyclouridine (PTAU) in improving the oral bioavailability of uridine. PTAU is a new potent and specific inhibitor

of uridine phosphorylase (UrdPase, EC 2.4.2.3), the enzyme responsible for uridine catabolism. This compound was designed as a lipophilic inhibitor in order to facilitate its access to the liver and intestine, the main organs involved in uridine catabolism. PTAU is not toxic to mice and is fully absorbed after oral administration (100% oral bioavailability). PTAU was administered orally to mice alone or with uridine. The plasma levels of PTAU as well as those of uridine and its catabolite uracil were measured using HPLC, and pharmacokinetic anal. was performed. Coadministration of PTAU with uridine elevated the concentration of plasma uridine in a dose-dependent manner over that resulting from the administration of the same dose of uridine alone, and reduced the clearance of uridine as well as the peak plasma concentration (Cmax) and area under the curve (AUC) of plasma uracil. Coadministration of PTAU at 30, 45 and 60 mg/kg improved the low oral bioavailability (7.7%) of uridine administered at 1320 mg/kg by 4.3-, 5.9- and 9.9-fold, resp., and reduced the AUC of plasma uracil (1227.8 $\mu\text{mol}\cdot\text{h/l}$) by 5.7-, 6.8- and 8.2-fold, resp. Similar results were observed when PTAU was coadministered with lower doses of uridine. Oral PTAU at 30, 45 and 60 mg/kg improved the oral bioavailability of 330 mg/kg uridine by 1.8-, 2.6- and 2.8-fold, and that of 660 mg/kg uridine by 2.2-, 2.6- and 3.2-fold, resp. The effectiveness of PTAU in improving the oral bioavailability of uridine could be useful in the rescue or protection from host toxicities of various chemotherapeutic pyrimidine analogs as well as in the management of medical disorders that are remedied by administration of uridine.

REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 20 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:675256 HCAPLUS

DOCUMENT NUMBER: 136:37875

TITLE: Asymmetric synthesis of carbocyclic pyrimidine nucleosides via π -allylpalladium complex

AUTHOR(S): Shi, Junxing; Schinazi, Raymond F.

CORPORATE SOURCE: Pharmasset, Inc., Tucker, GA, 30084, USA

SOURCE: Nucleosides, Nucleotides & Nucleic Acids (2001), 20(4-7), 1367-1370

CODEN: NNNAFY; ISSN: 1525-7770

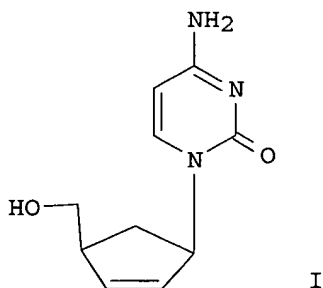
PUBLISHER: Marcel Dekker, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 136:37875

GI



AB Racemic and enantiomerically pure carbocyclic pyrimidine nucleosides, e.g.

I, were synthesized efficiently by a convergent approach using Trost nucleophilic addition of π -allylpalladium complexes.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 21 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:162762 HCAPLUS

DOCUMENT NUMBER: 133:70803

TITLE: Treatment of isografted 9L rat brain tumors with β -5-o-carboranyl-2'-deoxyuridine neutron capture therapy

AUTHOR(S): *Schinazi, Raymond F.*; Hurwitz, Selwyn J.; Liberman, Irina; Juodawlkis, Amy S.; Tharnish, Phillip; *Shi, Junxing*; Liotta, Dennis C.; Coderre, Jeffrey A.; Olson, Jeffrey

CORPORATE SOURCE: Department of Pediatrics, Laboratory of Biochemical Pharmacology, Emory University School of Medicine, Atlanta, GA, 30322, USA

SOURCE: Clinical Cancer Research (2000), 6(2), 725-730
CODEN: CCREF4; ISSN: 1078-0432

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB β -5-O-Carboranyl-2'-deoxyuridine (D-CDU) is a nontoxic pyrimidine nucleoside analog designed for boron neutron capture therapy of brain tumors. In vitro studies indicated that D-CDU accumulates to levels 92- and 117-fold higher than the extracellular concentration in rat 9L and human U-251 glioma cells, resp., and persists for several hours at levels 5-fold higher than the extracellular concentration Furthermore, D-CDU was not toxic

to

rats injected i.p. with up to 150 mg/kg. On the basis of these studies, D-CDU was evaluated as a neutron capture therapy agent using rats bearing stereotactically implanted intracranial 9L tumors at single i.p. doses of 30 mg/kg and 150 mg/kg of D-CDU (20% 10B enriched), given 2 h before irradiation with thermal neutrons. Boron concns. in tumors 2 h after dosing were 2.3 ± 1.6 and 7.4 ± 1.3 μ g boron/g tissue (mean \pm SD), corresponding to tumor/brain ratios of 11.5 ± 3.6 and 6.8 ± 2.0 μ g boron/g tissue for the low and high doses, resp. All untreated animals died within 28 days, whereas half survived at days 32, 55, and 38 for groups receiving neutrons only, 30 mg/kg D-CDU, and 150 mg/kg D-CDU, resp. Odds ratios of all treatment groups differed significantly from the untreated group ($P < 0.002$; logrank test). The median survival time for the 30 mg/kg-treated group but not for the 150 mg/kg-treated group was significantly longer than for rats treated with neutrons only ($P = 0.036$), which may correlate with the decreased tumor selectivity for D-CDU observed at the higher dose. Addnl. pharmacodynamic studies are warranted to determine optimal dosing strategies for D-CDU.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 22 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:601103 HCAPLUS

DOCUMENT NUMBER: 131:317323

TITLE: Mechanistic studies show that (-)-FTC-TP is a better inhibitor of HIV-1 reverse transcriptase than 3TC-TP

AUTHOR(S): Feng, Joy Y.; *Shi, Junxing*; *Schinazi, Raymond F.*; Anderson, Karen S.

CORPORATE SOURCE: Department of Pharmacology, Yale University School of Medicine, New Haven, CT, 06520-8066, USA

SOURCE: FASEB Journal (1999), 13(12), 1511-1517
 CODEN: FAJOEC; ISSN: 0892-6638
 PUBLISHER: Federation of American Societies for Experimental
 Biology
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Of all of the nucleoside inhibitors approved by the FDA for treatment of AIDS, (-)- β -2',3'-dideoxy-3'-thiacytidine (3TC, lamivudine) is the only one with the unnatural (-)- β -L configuration. The fluorinated derivative (-)- β -2',3'-dideoxy-5-fluoro-3'-thiacytidine [(-)-FTC] and its triphosphate form have also been reported to have excellent antiretroviral activity against HIV-1 reverse transcriptase (RT). Preliminary results of clin. trials suggest that (-)-FTC is 6- to 10-fold more potent than 3TC. However, the mol. mechanism for the observed enhanced clin. potency of (-)-FTC to inhibit viral replication is not understood. The present mechanistic studies used a transient kinetic approach and were designed to compare the incorporation of 3TC-TP and (-)-FTC-TP into DNA by HIV-1 RT and illuminate key features that may play a role in the differential potency. Here we show that (-)-FTC-TP is incorporated 10-fold more efficiently than 3TC-TP during HIV-1 RT-catalyzed RNA-dependent DNA synthesis. The enhanced incorporation efficiency of (-)-FTC-TP may be a key mechanistic feature that, in part, is responsible for the enhanced potency of (-)-FTC observed in ongoing clin. trials.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

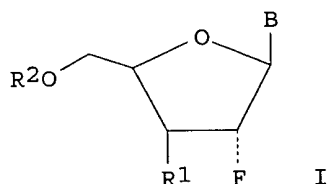
L40 ANSWER 23 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:566061 HCAPLUS
 DOCUMENT NUMBER: 131:170587
 TITLE: Preparation of 2'-fluoro nucleosides as antiviral agents
 INVENTOR(S): *Schinazi, Raymond F.*; Liotta, Dennis C.;
 Chu, Chung K.; Mcatee, J. Jeffrey; *Shi, Junxing*; Choi, Yongseok; Lee, Kyeong; Hong, Joon H.
 PATENT ASSIGNEE(S): Emory University, USA; The University of Georgia Research Foundation, Inc.
 SOURCE: PCT Int. Appl., 109 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943691	A1	19990902	WO 1999-US4051	19990225
W:	AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2322008	AA	19990902	CA 1999-2322008	19990225
AU 9927871	A1	19990915	AU 1999-27871	19990225
EP 1058686	A1	20001213	EP 1999-908437	19990225
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, RO			

JP 2002504558	T2	20020212	JP 2000-533443	19990225
US 6348587	B1	20020219	US 1999-257130	19990225
BR 9908270	A	20040629	BR 1999-8270	19990225
US 2002198171	A1	20021226	US 2002-61128	20020130
US 6911424	B2	20050628		
AU 2003244569	A1	20031002	AU 2003-244569	20030905
US 2004254141	A1	20041216	US 2004-796529	20040308
PRIORITY APPLN. INFO.:			US 1998-75893P	P 19980225
			US 1998-80569P	P 19980403
			US 1999-257130	A1 19990225
			WO 1999-US4051	W 19990225
			US 2002-61128	A1 20020130

OTHER SOURCE(S): MARPAT 131:170587
GI



AB 2'-Fluoro nucleoside compds. I wherein R1 is OH, H, OR3, N3, CN, halogen, including F, or CF3, lower alkyl, amino, lower alkylamino, or alkoxy, and base refers to a purine or pyrimidine base; R2 is H, phosphate, including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug; acyl, or other pharmaceutically acceptable leaving group which when administered in vivo, is capable of providing a compound wherein R2 is H or phosphate; sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl, benzyl, wherein the Ph group is optionally substituted with one or more substituents as described in the definition of aryl given above, a lipid, an amino acid, peptide, or cholesterol; and R3 is acyl, alkyl, phosphate, or other pharmaceutically acceptable leaving group which when administered in vivo, is capable of being cleaved to the parent compound, or a pharmaceutically acceptable salt thereof, are disclosed which are useful in the treatment of hepatitis B infection, hepatitis C infection, HIV and abnormal cellular proliferation, including tumors and cancer. Thus, 1-(2,3-dideoxy-2-fluoro-β-L-glycero-pent-2-eno-furanosyl)thymine was prepared and tested for its antiviral activity (EC50 > 100 μM).

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 24 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:409646 HCAPLUS

DOCUMENT NUMBER: 131:130169

TITLE: Nucleic acids and nucleosides containing carboranes

AUTHOR(S): Lesnikowski, Zbigniew J.; Shi, Junxing;

Schinazi, Raymond F.

CORPORATE SOURCE: Laboratory of Molecular Virology and Biological Chemistry, Center of Microbiology and Virology, Lodz, Pol.

SOURCE: Journal of Organometallic Chemistry (1999), 581(1-2), 156-169

CODEN: JORCAI; ISSN: 0022-328X

PUBLISHER: Elsevier Science S.A.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 84 refs. on the bioorg. chemical of nucleic acids and nucleosides containing carboranes. The use of carboranyl cluster as a modifying entity for nucleosides and oligonucleotides presents a new concept in the chemical of nucleic acids and nucleic acids' components, and facilitates studies on new DNA based, carborane-containing materials and pharmaceuticals. Synthesis, physicochem. and biol. properties of these new nucleosides and nucleic acids modifications are described.

REFERENCE COUNT: 84 THERE ARE 84 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 25 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:120304 HCAPLUS

DOCUMENT NUMBER: 130:223527

TITLE: Synthesis and Biological Evaluation of
2',3'-Didehydro-2',3'-dideoxy-5- fluorocytidine (D4FC)
Analog: Discovery of Carbocyclic Nucleoside
Triphosphates with Potent Inhibitory Activity against
HIV-1 Reverse Transcriptase

AUTHOR(S): Shi, Junxing; McAtee, J. Jeffrey; Wirtz,
Susan Schlueter; Tharnish, Phillip; Juodawlkis, Amy;
Liotta, Dennis C.; Schinazi, Raymond F.

CORPORATE SOURCE: Departments of Pediatrics and Chemistry, Emory
University, Atlanta, GA, 30322, USA

SOURCE: Journal of Medicinal Chemistry (1999), 42(5), 859-867
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The discovery of a novel cytosine nucleoside, β -D-2',3'-didehydro-2',3'-dideoxy-5-fluorocytidine (D-D4FC), as a potent antihuman immunodeficiency virus (HIV) agent led us to synthesize a series of analogs and derivs. of β -D-D4FC that could be more selective and also possess increased glycosidic bond stability. The synthesized D-D4FC analogs were evaluated for anti-HIV-1 activity, anticancer activity, and cytotoxicity in various cells. The biol. data demonstrated that the 5-substitution of β -D-D4FC with bromine and iodine resulted in the loss of antiviral activity, and the α -D anomer of D-D4FC was also devoid of activity. The 5-fluorouracil analogs of D-D4FC were less potent and more cytotoxic than the parent compound, whereas the β -L-D4FU showed both potent anti-HIV-1 activity and cytotoxicity. N4- and 5'-O-acyl derivs. of β -D-D4FC exhibited comparable antiviral activity to β -D-D4FC. In contrast, the N4-iso-Pr derivative of β -D-D4FC was not active against HIV-1, even at 100 μ M. The carbocyclic analogs of D4FC demonstrated weak activity against HIV-1 and no toxicity in various cells. The triphosphates of the carbocyclic nucleosides demonstrated potent inhibitory activity against recombinant HIV-1 reverse transcriptase at submicromolar concns. Of the compds. tested as potential anticancer agents, β -D-, α -D-, and β -L-D4FU showed inhibitory activity against rat glioma and modest activity against human lung carcinoma, lymphoblastoid, and skin melanoma cells.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 26 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:99600 HCAPLUS

DOCUMENT NUMBER: 130:291051

TITLE: Pharmacokinetics of the antiviral agent
 β -D-2',3'-didehydro-2',3'-dideoxy-5-fluorocytidine in Rhesus monkeys

AUTHOR(S): Ma, Li; Hurwitz, Selwyn J.; *Shi, Junxing*;
Mcatee, Jeffrey J.; Liotta, Dennis C.; McClure, Harold
M.; *Schinazi, Raymond F.*

CORPORATE SOURCE: Department of Pediatrics, Emory University, Decatur,
GA, 30033, USA

SOURCE: Antimicrobial Agents and Chemotherapy (1999), 43(2),
381-384
CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The pharmacokinetic parameters of the title nucleoside antiretroviral agent (D-D4FC) in rhesus monkeys were determined with a 2-compartment model after the administration of a single dose. The average values for the terminal half-life, renal clearance, and total systemic clearance after i.v. administration were 3.6 h, 0.31 L/kg/h and 0.43 L/kg/h, resp. The oral bioavailability of D-D4FC averaged 41%. After i.v. administration, 76% of the compound was recovered intact in the urine within 8 h, indicating that D-D4FC was eliminated mainly by renal excretion. D-D4FC was detected in the cerebrospinal fluid (CSF) at similar concns. after administration by both the i.v. and oral routes. D-D4FC levels in plasma and CSF were higher than the median effective concentration for human immunodeficiency virus type 1 in vitro.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 27 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:225294 HCAPLUS

DOCUMENT NUMBER: 128:270626

TITLE: Unexpected formation of novel butenolides by
thermolysis of o-carboranyl substituted cyclobutenones

AUTHOR(S): Goudgaon, Naganna M.; *Shi, Junxing*;
Schinazi, Raymond F.

CORPORATE SOURCE: Veterans Affairs Medical Center, Decatur, GA, 30033,
USA

SOURCE: Tetrahedron Letters (1998), 39(14), 1869-1872
CODEN: TELEAY; ISSN: 0040-4039

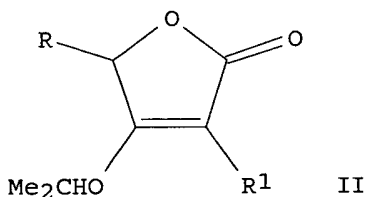
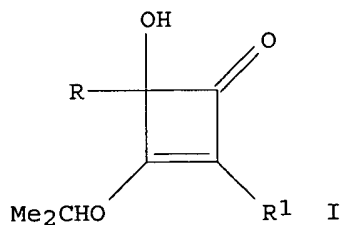
PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 128:270626

GI



AB On thermolysis, o-carboranyl-substituted 4-aryl-4-hydroxycyclobutenones I

(R = Ph, thienyl, furyl, 2-MeOC₆H₄; R₁ = o-carboranyl) undergo electrocyclic ring opening followed by ring closure to yield substituted butenolides II (same R, R₁). This is in contrast to the thermolysis of cyclobutenones which generally produces substituted quinones.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 28 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:211892 HCAPLUS

DOCUMENT NUMBER: 128:308686

TITLE: Synthesis and biological properties of the four optical isomers of 5-o-carboranyl-2',3'-dideohydro-2',3'-dideoxyuridine

AUTHOR(S): Graciet, Jean-Christophe G.; *Shi, Junxing*; *Schinazi, Raymond F.*

CORPORATE SOURCE: Atlanta Veterans Affairs Medical Cent., Decatur, GA, 30033, USA

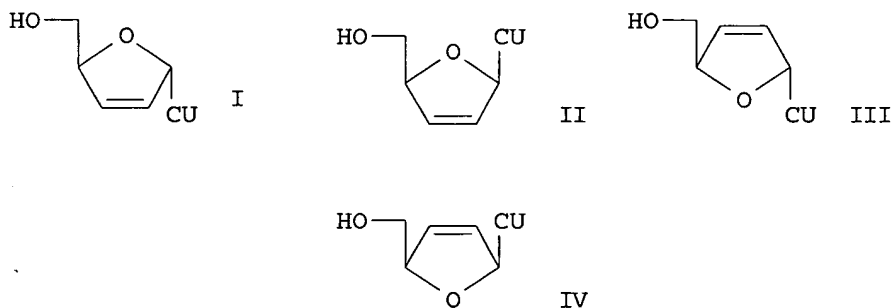
SOURCE: Nucleosides & Nucleotides (1998), 17(4), 711-727
CODEN: NUNUD5; ISSN: 0732-8311

PUBLISHER: Marcel Dekker, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB The four title stereoisomers I-IV (CU = 5-o-carboranylluracil) were prepared and their antiviral activity and cytotoxicity in normal and cancer human cells determined. Coupling of silylated 5-o-carboranylluracil with protected D/L 2,3-dideoxy-2-phenylselenenylribosylacetates provided after oxidative elimination and deprotection, the desired compds. The presence of the electron deficient 5-o-carboranyl moiety on uracil influenced the yield of the various isomers. In general, the compds. demonstrated weak anti-human immunodeficiency virus activity in primary human lymphocytes. No marked difference in the biol. profile was noted for the various optical isomers, suggesting that the high lipophilicity of these nucleosides imparted by the carboranyl moiety overrides stereochem. considerations in the 2',3'-dideohydro-2',3'-dideoxyglycon moiety.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 29 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:138749 HCAPLUS

TITLE: Chiral liquid chromatographic separation of

3'-heteronucleosides on amylose chiral stationary phase and their anti-HIV activity in human lymphocytes.

AUTHOR(S): Ma, L.; Shi, J.; Chu, C. K.; Schinazi, R. F.

CORPORATE SOURCE: School Medicine, Emory University, Decatur, GA, 30033, USA

SOURCE: Book of Abstracts, 215th ACS National Meeting, Dallas, March 29-April 2 (1998), CARB-063. American Chemical Society: Washington, D. C.
CODEN: 65QTAA

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB Many enantiomeric compds. often have different activities in biol. systems since they interact with receptors or enzymes that are chiral. While one enantiomer has antiviral activity, the other enantiomer may be toxic or inactive in various biol. systems. Therefore, it is necessary to resolve each enantiomer and to characterize them biol. An inclusion chromatog. chiral column, ChiralPak AS, was employed for the separation of enantiomers of 2',3'-dideoxy-5-fluoro-3'-thiacytidine (FTC) and its selenium analog (Se-FddC). When the mobile phase is 100% 2-propanol, the resolution factors were 1.91, 3.28, and 2.87 for α -Se-FddC, β -Se-FddC and β -FTC, resp. The results indicated that both steric and electrostatic factors contribute to the chiral recognition, but steric factors play a major role in the chiral separation. In HIV-1 infected primary human lymphocytes, (-)- β -Se-FddC (mean EC50 = 0.21 μ M) was 200-fold more potent than the (+)- β -counterpart, and demonstrated no cytotoxicity in various cells.

L40 ANSWER 30 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:486035 HCAPLUS

TITLE: Synthesis and biological activities of optical isomers of 5-O-carboranyl-2',3'-didehydro-2',3'-dideoxyuridine (D4CU).

AUTHOR(S): Shi, J.; Graciet, J. -C. G.; Schinazi, R. F.

CORPORATE SOURCE: VA Medical Center, Decatur, GA, 30033, USA

SOURCE: Book of Abstracts, 214th ACS National Meeting, Las Vegas, NV, September 7-11 (1997), CARB-079. American Chemical Society: Washington, D. C.
CODEN: 64RNAO

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB The four isomers of the 5-o-carboranyl-2',3'-didehydro-2',3'-dideoxyuridine (D4CU) were synthesized, fully characterized, and evaluated for antiviral and cytotoxicity. The coupling of silylated 5-o-carboranyluracil with the protected D/L 2,3-dideoxy-2-phenylselenenylribosylacetates, which were derived from the two optically pure enantiomers of dihydro-5-hydroxymethyl-2(3H)-furanone, provided after oxidative elimination and deprotection, the desired compds. The presence of the electron deficient 5-o-carboranyl moiety on uracil unexpectedly influenced the ratios of the various isomers, suggesting interaction of the carboranyl moiety with the phenylselenenyl group. The synthesized compds. were evaluated for their antiviral activity against HIV-1, and for their cytotoxicity in various mammalian cells. In general, the compds. demonstrated modest anti-HIV activity in human lymphocytes. Surprisingly, no marked difference in biol. profile was noted for the various enantiomers suggesting that the high lipophilicity of these nucleosides, imparted by the carboranyl moiety, overrides stereochem. considerations in

the 2',3'-didehydro-aglycon moiety.

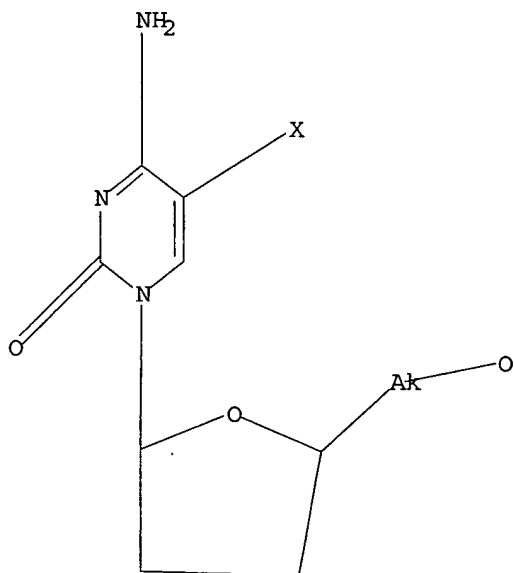
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L2 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

L4 109180 SEA FILE=REGISTRY SSS FUL L2
L10 12372 SEA FILE=HCAPLUS ABB=ON PLU=ON (HCV+PFT/CT OR "CLASSICAL
SWINE FEVER VIRUS"+PFT/CT OR "HEPATITIS C VIRUS"+PFT/CT)
L11 11667 SEA FILE=HCAPLUS ABB=ON PLU=ON "HEPATITIS C VIRUS"+PFT/CT
L12 15162 SEA FILE=HCAPLUS ABB=ON PLU=ON (HCV OR H(1A)C(1A)V OR
HEPATITIS C VIRUS?)/OBI,BI
L13 90130 SEA FILE=HCAPLUS ABB=ON PLU=ON ((VIRAL?)/OBI,BI
L14 55395 SEA FILE=HCAPLUS ABB=ON PLU=ON (ANTIVIRAL?)/OBI,BI
L20 STR



Structure attributes must be viewed using STN Express query preparation.

L22 779 SEA FILE=REGISTRY SUB=L4 SSS FUL L20
L23 279 SEA FILE=CAPLUS ABB=ON PLU=ON L22 (L) (PAC OR THU OR BAC OR
PKT OR DMA)/RL
L24 20 SEA FILE=HCAPLUS ABB=ON PLU=ON L23 AND (L10 OR L11 OR L12)
L27 168 SEA FILE=HCAPLUS ABB=ON PLU=ON L23 AND (L10 OR L11 OR L12 OR
L13 OR L14)
L30 59 SEA FILE=HCAPLUS ABB=ON PLU=ON L27 AND (HEPATITIS? OR HCV?
OR H(1A)C(1A)V?)
L33 20 SEA FILE=HCAPLUS ABB=ON PLU=ON L30 AND L24
L34 59 SEA FILE=HCAPLUS ABB=ON PLU=ON (L30 OR L33)

=> d ibib abs hitind hitstr l34 tot

L34 ANSWER 1 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1328666 HCAPLUS

DOCUMENT NUMBER: 144:50033
 TITLE: Vaccine compositions diminishing side effects
 INVENTOR(S): Buller, Robert Mark L.
 PATENT ASSIGNEE(S): Saint Louis University, USA
 SOURCE: PCT Int. Appl., 30 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005121378	A2	20051222	WO 2005-US18682	20050526
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2004-576840P P 20040603

AB The invention provides kits, methods and compns. of matter which improve the safety of vaccination. By combining the administration of **antiviral** drugs, particularly ester derivs. of cidofovir, with the administration of viral vaccines, particularly the variola vaccine DryVax, side effects of the vaccine are diminished without significantly affecting the effectiveness of the vaccine.

IC ICM C12Q001-70

CC 15-2 (Immunochemistry)

Section cross-reference(s): 1

ST vaccine **viral** infection **antiviral** agent side effect;
 smallpox vaccine DryVax cidofovir side effect

IT **Antiviral** agents

Bordetella pertussis

Clostridium tetani

Corynebacterium diphtheriae

Hepatitis A virus

Hepatitis B virus

Human

Human herpesvirus 3

Human immunodeficiency virus

Human poliovirus

Influenza virus

Measles virus

Mumps virus

Rabies virus

Rubella virus

Streptococcus pneumoniae

T cell (lymphocyte)

Vaccines

Variola virus

(administration of **antiviral** drugs with **viral**
 vaccines diminishes adverse side effects)

IT Antibodies and Immunoglobulins
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (administration of **antiviral** drugs with **viral**
 vaccines diminishes adverse side effects)

IT Nucleoside analogs
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (administration of **antiviral** drugs with **viral**
 vaccines diminishes adverse side effects)

IT Neisseria meningitidis
 (group C; administration of **antiviral** drugs with
viral vaccines diminishes adverse side effects)

IT Skin, disease
 (lesion; administration of **antiviral** drugs with **viral**
 vaccines diminishes adverse side effects)

IT Haemophilus influenzae
 (type b; administration of **antiviral** drugs with **viral**
 vaccines diminishes adverse side effects)

IT Infection
 (variola; administration of **antiviral** drugs with
viral vaccines diminishes adverse side effects)

IT Infection
 (**viral**; administration of **antiviral** drugs with
viral vaccines diminishes adverse side effects)

IT 54-42-2, Idoxuridine 70-00-8, Trifluridine 127-07-1, Hydroxyurea
 548-04-9, Hypericin 661-19-8, n-Docosanol 768-94-5, Amantadine
 3056-17-5, Stavudine 4428-95-9, Foscarnet 5536-17-4, Vidarabine
 7481-89-2, Zalcitabine 9025-10-9, Adenylate deaminase 13392-28-4,
 Rimantadine 15185-43-0, DOTC 25526-93-6, Alovudine 29321-75-3, PRO
 2000 30516-87-1, Zidovudine 36791-04-5, Ribavirin 39809-25-1,
 Penciclovir 59277-89-3, Acyclovir **69123-90-6**, Fiacitabine
 69123-98-4, Fialuridine 69304-47-8, Brivudin 69655-05-6, Didanosine
 72599-27-0, SC-48334 77181-69-2, Sorivudine 82410-32-0, Ganciclovir
 84472-85-5, AZdU 84558-93-0, Netivudine 87190-79-2, CS-92 99011-02-6
 , Imiquimod 104227-87-4, Famciclovir 106941-25-7, Adefovir
 107355-45-3, WIN 54954 110143-10-7, Lodenosine 113852-37-2, Cidofovir
 113852-37-2D, Cidofovir, analogs 119644-22-3, 935U83 121104-96-9, MDL
 28574 122051-95-0, Lithium γ -linolenate 124436-59-5, Pirodavir
 124832-26-4, Valaciclovir 127757-45-3, Cyclic HPMPC 127759-89-1,
 Lobucavir 127779-20-8, Saquinavir 129618-40-2, Nevirapine
 131707-23-8, Arbidol 134678-17-4, Lamivudine 134878-17-4, A-77003
 135525-78-9, L-697661 136470-78-5, Abacavir 136817-59-9, Delavirdine
 137332-54-8, Tivirapine 138540-32-6, Ateviridine mesylate 139110-80-8,
 Zanamivir 139694-65-8, RPI 312 141790-23-0, Fozivudine tidoxil
 142217-69-4, Entecavir 142340-99-6, Adefovir dipivoxil 142632-32-4,
 Calanolide A 143224-34-4, SC-52151 143491-57-0, Emtricitabine
 144875-48-9, Resiquimod 145514-04-1, DAPD 147127-20-6, Tenofovir
 147318-81-8, KNI-272 147362-57-0, Loviride 148465-45-6, SP-303
 149394-65-0, U-96988 149488-17-5, Troviridine 149950-60-7, Emivirine
 150378-17-9, Indinavir 151867-81-1, DMP-323 153021-75-1, GEM 91
 153168-05-9, Pleconaril 154598-52-4, Efavirenz 154719-23-0, ISIS 5320
 155148-31-5, AMD 3100 155213-67-5, Ritonavir 159519-65-0, T-20
 159989-64-7, Nelfinavir 160369-77-7, Fomivirsen sodium 161814-49-9,
 Amprenavir 163451-80-7, HBY 097 164514-52-7, SDZ PRI 053
 166335-18-8, U-103017 171345-51-0, AR177 173720-57-5, GEM 132
 174391-92-5, Mozenavir 174484-41-4, Tipranavir 175385-62-3, Lasinavir
 176161-24-3, Maribavir 177932-89-7, DMP-450 178040-94-3, GW 420867X
 178979-85-6, Capravirine 192725-17-0, ABT-378 195156-77-5,
 Valomaciclovir stearate 196618-13-0, Oseltamivir 198904-31-3,
 BMS-232632 202138-50-9, Tenofovir disoproxil fumarate 217950-62-4, GW

275175X 223537-30-2, AG7088 226700-79-4, GW 433908 231957-54-3,
MIV-150 251562-00-2, T-1249 269055-15-4, R165335 282104-12-5, PD
178390 444805-26-9, Octadecyloxyethyl cidofovir 444805-28-1,
Hexadecyloxypropyl cidofovir 860435-79-6, Dryvax 871303-71-8, PETT 5
871377-04-7

RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(administration of **antiviral** drugs with **viral**
vaccines diminishes adverse side effects)

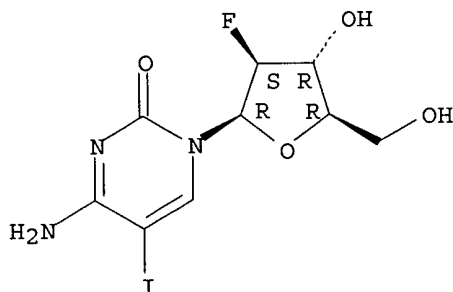
IT 69123-90-6, Fiacitabine

RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(administration of **antiviral** drugs with **viral**
vaccines diminishes adverse side effects)

RN 69123-90-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-
5-iodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L34 ANSWER 2 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:185375 HCAPLUS

DOCUMENT NUMBER: 142:254563

TITLE: Antimetabolite **antiviral** dosing regimen for
hepatitis C virus or
flaviviridae therapy

INVENTOR(S): Stuyver, Lieven J.

PATENT ASSIGNEE(S): Belg.

SOURCE: U.S. Pat. Appl. Publ., 23 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005049220	A1	20050303	US 2004-921052	20040818
PRIORITY APPLN. INFO.:			US 2003-496202P	P 20030818

AB An anti-**hepatitis C** agent which is an antimetabolite to the host
and cannot be administered on a daily or chronic basis as is usual in
antiviral therapy (referred to below as an "anti-**HCV**
antimetabolite"), can be administered using a traditional anticancer
dosing regimen (for example via i.v. or parenteral injection), over a
period of 1-7 days followed by cessation of therapy until rebound of the
viral load is noted. This dosing regimen runs counter to conventional
antiviral experience, wherein effective agents are usually

administered over at least fourteen days of sustained therapy, and typically on an indefinite daily basis.

- IC ICM A61K031-7072
ICS A61K031-66; A61K031-513; A61K031-525; A61K031-522
- INCL 514049000; 514251000; 514263300; 514269000; 514283000; 514114000; 514449000
- CC 1-5 (Pharmacology)
Section cross-reference(s): 63
- ST antimetabolite **antiviral** dosing regimen **hepatitis C virus** flaviviridae therapy
- IT Replicon
(HCV replicon system; antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)
- IT Genetic element
RL: BSU (Biological study, unclassified); BIOL (Biological study) (IRES (internal ribosomal entry site) element, inhibitor of IRES-dependent translation, combination; antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)
- IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study) (RNA helicase, inhibitors, combination; antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)
- IT Nucleotides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (analogs, combination; antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)
- IT **Antiviral** agents
Border disease virus 1
Bovine diarrhea virus
Combination chemotherapy
Dengue virus
Flaviviridae
Hepatitis C virus
Human
West Nile virus
Yellow fever virus
(antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)
- IT RNA
RL: BSU (Biological study, unclassified); BIOL (Biological study) (antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)
- IT Polyoxyalkylenes, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)
- IT Cytotoxic agents
(antimetabolites; antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)
- IT Phosphorothioate oligonucleotides
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (antisense, combination; antimetabolite **antiviral** dosing

regimen for **hepatitis C virus** or
flaviviridae therapy)

IT Interferons
Interleukins
Ribozymes
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(combination; antimetabolite **antiviral** dosing regimen for
hepatitis C virus or flaviviridae therapy)

IT Drug delivery systems
(injections, i.v.; antimetabolite **antiviral** dosing regimen
for **hepatitis C virus** or flaviviridae
therapy)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(natural, combination; antimetabolite **antiviral** dosing
regimen for **hepatitis C virus** or
flaviviridae therapy)

IT Drug delivery systems
(oral; antimetabolite **antiviral** dosing regimen for
hepatitis C virus or flaviviridae therapy)

IT Drug delivery systems
(parenterals; antimetabolite **antiviral** dosing regimen for
hepatitis C virus or flaviviridae therapy)

IT Antisense oligonucleotides
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(phosphorothioate, combination; antimetabolite **antiviral**
dosing regimen for **hepatitis C virus** or
flaviviridae therapy)

IT Infection
(**viral**; antimetabolite **antiviral** dosing regimen for
hepatitis C virus or flaviviridae therapy)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(τ , combination; antimetabolite **antiviral** dosing regimen
for **hepatitis C virus** or flaviviridae
therapy)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(α , combination; antimetabolite **antiviral** dosing
regimen for **hepatitis C virus** or
flaviviridae therapy)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(α , α con-1, combination; antimetabolite **antiviral**
dosing regimen for **hepatitis C virus** or
flaviviridae therapy)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(α -2a, pegylated, combination; antimetabolite **antiviral**
dosing regimen for **hepatitis C virus** or
flaviviridae therapy)

IT Interferons

- RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(γ, combination; antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)
- IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(δ, combination; antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)
- IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ω, combination; antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)
- IT 95058-81-4, Gemcitabine 122111-03-9, Gemcitabine hydrochloride
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)
- IT 9012-49-1, Aspartate transcarbamoylase 9023-56-7, CTP synthase
9024-62-8, Orotidine monophosphate decarboxylase 9028-93-7, Inosine monophosphate dehydrogenase 9029-03-2, Dihydroorotate dehydrogenase
9031-61-2, Thymidylate synthase 9040-57-7, Ribonucleotide reductase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)
- IT 50-44-2, 6-Mercaptopurine 50-91-9, 2'-Deoxy-5-fluorouridine 51-21-8, 5-Fluorouracil 54-25-1, 6-Azauridine 57-22-7, Vincristine 59-05-2, Methotrexate 70-51-9, Deferoxamine 127-07-1, Hydroxyurea 147-94-4, Cytosine arabinoside 154-42-7, 6-Thioguanine 320-67-2, 5-Azacytidine 446-86-6, Azathioprine 611-53-0, Ibacitabine 865-21-4, Vinblastine 1455-77-2, Guanazole 2353-33-5, Decitabine 4291-63-8, Cladribine 7481-89-2, Zalcitabine 21679-14-1, Fludarabine 23205-42-7 24280-93-1, Mycophenolic acid 25322-68-3D, PEG, conjugates with interferon α2a 27089-56-1, 2-Thio-6-azauridine 29767-20-2, Teniposide 30868-30-5, Pyrazofurin 33419-42-0, Etoposide 36417-16-0, Dichloroallyl lawsone 50924-49-7, Mizoribine 51321-79-0 53910-25-1, 2'-Deoxycytosine 60084-10-8, Tiazofurin 61825-94-3, Oxaliplatin 69123-90-6, Fiacitabine 90597-22-1, Cyclopentenylcytosine 96187-53-0, Brequinar 112887-68-0, Raltitrexed 114248-23-6 130306-02-4 134419-26-4 154361-50-9, Capecitabine 244242-36-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)
- IT 67-99-2, Gliotoxin 84-11-7, Phenanthrenequinone 93-98-1D, Benzanilide, derivs. 504-78-9D, Thiazolidine, derivs. 17397-89-6, Cerulenin 36791-04-5, Ribavirin 98059-61-1 145258-61-3, Interferon β1 (human fibroblast protein moiety) 472960-22-8, Albuferon
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination; antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)
- IT 9026-28-2, RNA-dependent RNA polymerase 37353-41-6, Cysteine protease 149885-80-3, NS3 protease
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(inhibitors, combination; antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)

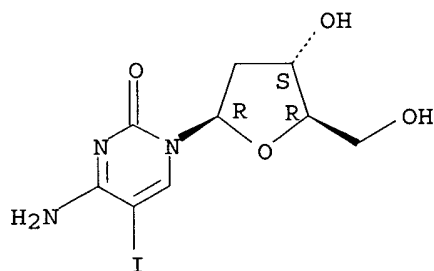
IT 611-53-0, Ibacitabine 69123-90-6, Fiacitabine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)

RN 611-53-0 HCAPLUS

CN Cytidine, 2'-deoxy-5-iodo- (7CI, 8CI, 9CI) (CA INDEX NAME)

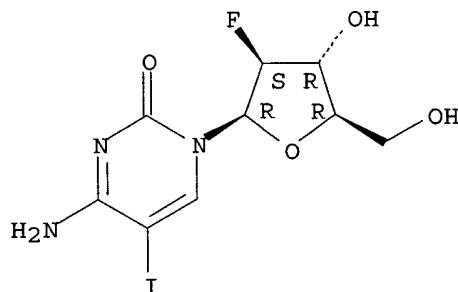
Absolute stereochemistry.



RN 69123-90-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-5-iodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L34 ANSWER 3 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:177803 HCAPLUS

DOCUMENT NUMBER: 142:254560

TITLE: Antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy

INVENTOR(S): Stuyver, Lieven J.

PATENT ASSIGNEE(S): Pharmasset, Inc., USA

SOURCE: PCT Int. Appl., 61 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005018330	A1	20050303	WO 2004-US26686	20040817
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:

US 2003-496202P P 20030818

AB An anti-**hepatitis C** agent which is an anti-metabolite to the host and cannot be administered on a daily or chronic basis as is usual in anti-viral therapy (referred to below as an "anti-**HCV** anti-metabolite"), can be administered using a traditional anti-cancer dosing regimen (for example via i.v. or parenteral injection), over a period of 1-7 days followed by cessation of therapy until rebound of the viral load is noted. This dosing regimen runs counter to conventional **antiviral** experience, wherein effective agents are usually administered over at least fourteen days of sustained therapy, and typically on an indefinite daily basis.

IC ICM A01N055-02

ICS A01N043-90; A01N043-38; A61K031-50

CC 1-5 (Pharmacology)

Section cross-reference(s): 63

ST antimetabolite **antiviral** dosing regimen **hepatitis C virus** flaviviridae therapy

IT Replicon

(**HCV** replicon system; antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)

IT Genetic element

RL: BSU (Biological study, unclassified); BIOL (Biological study) (IRES (internal ribosomal entry site) element, inhibitor of IRES-dependent translation, combination; antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)

IT Enzymes, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study) (RNA helicase, inhibitors, combination; antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)

IT Nucleotides, biological studies

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (analogs, combination; antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)

IT **Antiviral** agents

Border disease virus 1
 Bovine diarrhea virus
 Combination chemotherapy
 Dengue virus
 Flaviviridae

Hepatitis C virus

Human

West Nile virus

Yellow fever virus

(antimetabolite **antiviral** dosing regimen for
hepatitis C virus or flaviviridae therapy)

IT RNA

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antimetabolite **antiviral** dosing regimen for
hepatitis C virus or flaviviridae therapy)

IT Polyoxyalkylenes, biological studies

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(antimetabolite **antiviral** dosing regimen for
hepatitis C virus or flaviviridae therapy)

IT Cytotoxic agents

(antimetabolites; antimetabolite **antiviral** dosing regimen for
hepatitis C virus or flaviviridae therapy)

IT Phosphorothioate oligonucleotides

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(antisense, combination; antimetabolite **antiviral** dosing
regimen for **hepatitis C virus** or
flaviviridae therapy)

IT Interferons

Interleukins

Ribozymes

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(combination; antimetabolite **antiviral** dosing regimen for
hepatitis C virus or flaviviridae therapy)

IT Drug delivery systems

(injections, i.v.; antimetabolite **antiviral** dosing regimen
for **hepatitis C virus** or flaviviridae
therapy)

IT Interferons

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(natural, combination; antimetabolite **antiviral** dosing
regimen for **hepatitis C virus** or
flaviviridae therapy)

IT Drug delivery systems

(oral; antimetabolite **antiviral** dosing regimen for
hepatitis C virus or flaviviridae therapy)

IT Drug delivery systems

(parenterals; antimetabolite **antiviral** dosing regimen for
hepatitis C virus or flaviviridae therapy)

IT Antisense oligonucleotides

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(phosphorothioate, combination; antimetabolite **antiviral**
dosing regimen for **hepatitis C virus** or
flaviviridae therapy)

IT Infection

(**viral**; antimetabolite **antiviral** dosing regimen for
hepatitis C virus or flaviviridae therapy)

IT Interferons

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

- (τ , combination; antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)
- IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α , combination; antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)
- IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α , α con-1, combination; antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)
- IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α -2a, pegylated, combination; antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)
- IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(γ , combination; antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)
- IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(δ , combination; antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)
- IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ω , combination; antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)
- IT 95058-81-4, Gemcitabine 122111-03-9, Gemcitabine hydrochloride
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)
- IT 9012-49-1, Aspartate transcarbamoylase 9023-56-7, CTP synthase 9024-62-8, Orotidine monophosphate decarboxylase 9028-93-7, Inosine monophosphate dehydrogenase 9029-03-2, Dihydroorotate dehydrogenase 9031-61-2, Thymidylate synthase 9040-57-7, Ribonucleotide reductase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antimetabolite **antiviral** dosing regimen for **hepatitis C virus** or flaviviridae therapy)
- IT 50-44-2, 6-Mercaptopurine 50-91-9, 2'-Deoxy-5-fluorouridine 51-21-8, 5-Fluorouracil 54-25-1, 6-Azauridine 57-22-7, Vincristine 59-05-2, Methotrexate 70-51-9, Deferoxamine 127-07-1, Hydroxyurea 147-94-4, Cytosine arabinoside 154-42-7, 6-Thioguanine 320-67-2, 5-Azacytidine 446-86-6, Azathioprine 611-53-0, Ibacitabine 865-21-4, Vinblastine 1455-77-2, Guanazole 2353-33-5, Decitabine 4291-63-8, Cladribine 7481-89-2, Zalcitabine 21679-14-1, Fludarabine 23205-42-7 24280-93-1, Mycophenolic acid 25322-68-3D, PEG, conjugates with

interferon α 2a 27089-56-1, 2-Thio-6-azauridine 29767-20-2,
Teniposide 30868-30-5, Pyrazofurin 33419-42-0, Etoposide 36417-16-0,
Dichloroallyl lawsone 50924-49-7, Mizoribine 51321-79-0 53910-25-1,
2'-Deoxycoformycin 60084-10-8, Tiazofurin 61825-94-3, Oxaliplatin
69123-90-6, Fiacitabine 90597-22-1, Cyclopentenylcytosine
96187-53-0, Brequinar 112887-68-0, Raltitrexed 114248-23-6
130306-02-4 134419-26-4 154361-50-9, Capecitabine 244242-36-2

RL: PAC (Pharmacological activity); THU (Therapeutic
use); BIOL (Biological study); USES (Uses)

(antimetabolite **antiviral** dosing regimen for
hepatitis C virus or flaviviridae therapy)

IT 67-99-2, Gliotoxin 84-11-7, Phenanthrenequinone 93-98-1D, Benzanilide,
derivs. 504-78-9D, Thiazolidine, derivs. 17397-89-6, Cerulenin
36791-04-5, Ribavirin 98059-61-1 145258-61-3, Interferon β 1
(human fibroblast protein moiety) 472960-22-8, Albuferon
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(combination; antimetabolite **antiviral** dosing regimen for
hepatitis C virus or flaviviridae therapy)

IT 9026-28-2, RNA dependent RNA polymerase 37353-41-6, Cysteine protease
149885-80-3, NS3 protease
RL: BSU (Biological study, unclassified); BIOL (Biological study)

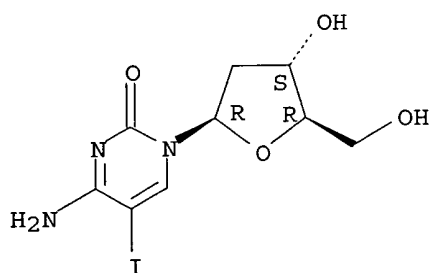
(inhibitors, combination; antimetabolite **antiviral** dosing
regimen for **hepatitis C virus** or
flaviviridae therapy)

IT 611-53-0, Ibacitabine **69123-90-6**, Fiacitabine
RL: PAC (Pharmacological activity); THU (Therapeutic
use); BIOL (Biological study); USES (Uses)
(antimetabolite **antiviral** dosing regimen for
hepatitis C virus or flaviviridae therapy)

RN 611-53-0 HCAPLUS

CN Cytidine, 2'-deoxy-5-iodo- (7CI, 8CI, 9CI) (CA INDEX NAME)

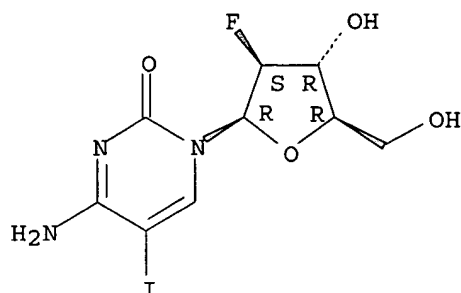
Absolute stereochemistry.



RN 69123-90-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy-2-fluoro- β -D-arabinofuranosyl)-
5-iodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 4 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:99157 HCAPLUS

DOCUMENT NUMBER: 142:170033

TITLE: Methods and compositions for the treatment or prevention of human immunodeficiency virus and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents

INVENTOR(S): Maziasz, Timothy

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 172 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005026902	A1	20050203	US 2004-769485	20040130
PRIORITY APPLN. INFO.:			US 2003-443910P	P 20030131

OTHER SOURCE(S): MARPAT 142:170033

AB The present invention provides compns. and methods for the treatment of human immunodeficiency virus (HIV) infection as well as HIV associated diseases and related disorders. More particularly, the invention provides a combination therapy for the treatment of HIV infection as well as HIV associated diseases and related disorders comprising the administration to a subject of an anti-human immunodeficiency virus agent in combination with a cyclooxygenase-2 selective inhibitor or an isomer or a pharmaceutically acceptable salt, ester, or prodrug thereof.

IC ICM A61K031-55

ICS A61K031-54

INCL 514217000; 514226500

CC 1-5 (Pharmacology)

ST HIV infection related condition treatment cyclooxygenase 2 inhibitor **antiviral**

IT AIDS (disease)

(-related complex; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)

IT CD4-positive T cell

T cell (lymphocyte)

(HIV infection reduces T-cells; methods and compns. for treatment or prevention of HIV infection and related conditions using

- cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT Sarcoma
(Kaposi's; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT Cell proliferation
(T cell, proliferation inhibitor as virucide; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT Muscle, disease
(ache; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT CD4 (antigen)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonist, as **viral** cellular entry inhibitor; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT Cytotoxic agents
(antimetabolites, in treatment regimen; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT Disease, animal
(arthropathy, aches; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT Acyclonucleosides
Nucleosides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as anti-HIV agent; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT Mycobacterium avium
(complex; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT Meningitis
(cryptococcal; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT Immunostimulants
(cyclooxygenase-2 inhibitor acts as an immunostimulant; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT Joint, anatomical
(disease, aches; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT T cell (lymphocyte)
(helper cell, HIV infection reduces T-cells; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT Infection
(herpes zoster; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)

- IT Antibiotics
- Antioxidants
- Antitumor agents
- Fungicides
- Immunomodulators
- Neoplasm
- Protozoacides
- Vaccines
 - (in treatment regimen; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT Antibodies and Immunoglobulins
- Cytokines
- Hormones, animal, biological studies
- Vitamins
- RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (in treatment regimen; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT Cytomegalovirus
- Human herpesvirus
 - (infection; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT Glycosylation
 - (inhibitor, as **viral** assembly inhibitor; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT AIDS (disease)
- Anti-AIDS agents
- Combination chemotherapy
- Diarrhea
- Drug delivery systems
- Fever and Hyperthermia
- Gene therapy
- Hepatitis**
- Human
- Human immunodeficiency virus
- Immunostimulation
- Lymphoma
- Seizures
 - (methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT Natural products, pharmaceutical
- RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT Antisense oligonucleotides
- RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT Pneumonia

- (pneumocystis carinii; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT Amines, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study) (polyamines, nonpolymeric, polyamine biosynthesis inhibitor as HIV inhibitor; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT **Viral** RNA
RL: BSU (Biological study, unclassified); BIOL (Biological study) (processing inhibitor, as **viral** assembly inhibitor; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT T cell (lymphocyte)
(proliferation, proliferation inhibitor as virucide; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT Skin, disease
(rash; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT Lymph node, disease
(swelling; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT Mouth, disease
(thrush; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT Infection
(toxoplasmosis; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT Infection
(**viral**; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (virion, antagonists as **viral** cellular entry inhibitor; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT Protein motifs
(zinc finger, inhibitor, as anti-HIV agent; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT 30220-45-2
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (0; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT 37205-61-1, Protease, inhibitor
RL: BSU (Biological study, unclassified); BIOL (Biological study) (as **viral** assembly inhibitor; methods and compns. for

- treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT 15687-27-1, Ibuprofen
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in treatment regimen; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT 9068-38-6, Reverse transcriptase 52350-85-3, Integrase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor, as anti-HIV agent; methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT 50-00-0, Formaldehyde, biological studies 111-30-8, Glutaral 548-04-9, Hypericin 2450-53-5, 3,5-Dicaffeoylquinic acid 6537-80-0 7770-78-7 13422-51-0, Hydroxocobalamin 19130-96-2, 1,5-Dideoxy-1,5-imino-D-glucitol 33419-42-0 79831-76-8 113852-37-2, Cidofovir 126456-36-8 126456-38-0 127749-96-6 127749-99-9 127779-20-8 138483-63-3 139694-65-8 140196-60-7 141804-42-4 142762-74-1 143224-34-4 144142-67-6 144779-91-9 146654-21-9 147318-81-8 147384-69-8 148314-61-8 149267-24-3 151867-81-1 153353-79-8 159142-13-9 159878-27-0 159878-28-1 159989-65-8 160231-42-5 161186-50-1 161277-26-5 161277-30-1 161277-32-3 164514-52-7 165591-25-3 165591-39-9 168394-24-9 168899-54-5 169273-51-2 169273-55-6 173261-21-7 173828-55-2 174484-41-4 177932-89-7 179409-87-1 180463-16-5 180902-22-1 183854-24-2 188762-00-7 192725-17-0 244641-43-8 329900-75-6, Cyclooxygenase-2 834911-92-1 834911-93-2 834911-94-3 834911-95-4 834911-96-5 834911-97-6 834911-98-7 834911-99-8 834912-00-4 834912-01-5 834912-02-6 834912-03-7 834912-04-8 834912-05-9 834912-06-0 834912-07-1 834912-08-2 834912-09-3 834912-10-6 834912-11-7 834912-12-8 834912-13-9 834912-14-0
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT 53-43-0, 3 β -Hydroxyandrost-5-en-17-one 472-15-1 534-76-9 1077-28-7, 1,2-Dithiolane-3-pentanoic acid 1093-91-0, 16- α -Bromo-3- β -hydroxyandrost-5-en-17-one 6060-06-6 21967-41-9 41135-06-2, Inophyllum B 60857-08-1, 12-Deoxyphorbol-13-acetate 76663-53-1, 13-Hydroxyingenol-3-(2,3-dimethylbutanoate)-13-dodecanoate 102674-90-8 110042-95-0, Acemannan 134332-63-1 135383-02-7 137793-81-8 137893-48-2 138667-71-7 142632-32-4, Calanolide A 142632-33-5, Calanolide B 149572-31-6, Conocurvone 152187-38-7, Inophyllum P 155213-67-5, Ritonavir 165460-07-1 174022-42-5, 3-O-(3',3'-Dimethylsuccinyl)betulinic acid 184539-38-6
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for treatment or prevention of HIV infection and related conditions using cyclooxygenase-2 selective inhibitors and **antiviral** agents)
- IT 98-10-2D, Benzenesulfonamide, analogs and compds. 103-82-2D, Phenylacetic acid, derivs. 127-07-1, Hydroxyurea 129-46-4 254-04-6D, 2H-1-Benzopyran, compds. 254-04-6D, Benzopyran, compds. and analogs 2054-35-5D, analogs 3056-17-5 3112-85-4D, Methylsulfonylbenzene, analogs and compds. 3416-05-5, 3'-Deoxythymidine 4097-22-7, 2',3'-Dideoxyadenosine 4431-00-9, Aurintricarboxylic acid 7057-48-9 7481-88-1 7481-89-2, 2',3'-Dideoxycytidine 14665-52-2, Bis(2-nitrophenyl)sulfone 25526-93-6, 3'-Fluoro-3'-deoxythymidine

29828-28-2D, Dihydronaphthalene, analogs 29968-14-7D, Dihydroquinoline, analogs 30516-87-1, 3'-Azido-3'-deoxythymidine 30516-87-1D, 3'-Azido-3'-deoxythymidine, 5'-alkylglycoside carbonates 31515-43-2, 2-Nitrophenyl phenyl sulfone 36791-04-5 41107-56-6, 3'-Fluoro-2',3'-dideoxyuridine 51246-79-8, 3'-Fluoro-2',3'-dideoxycytidine 51803-78-2 53766-80-6, 2',3'-Didehydro-2',3'-dideoxyguanosine 63585-09-1, Phosphonoformic acid trisodium salt 64224-21-1 66323-44-2 66323-46-4, 3'-Azido-2',3'-dideoxyguanosine 69655-05-6, 2',3'-Dideoxyinosine 71125-38-7 78794-60-2 79872-72-3 80937-31-1 84472-85-5, 3'-Azido-2',3'-dideoxyuridine 84472-89-9, 3'-Azido-2',3'-dideoxycytidine 85236-92-6, 3'-Azido-2',3'-dideoxy-5-iodouridine 85326-06-3, 2',3'-Dideoxyguanosine 85326-07-4, 6-Methyl-2',3'-dideoxyadenosine 87190-74-7, 3'-Azido-2',3'-dideoxy-5-fluorouridine 87190-79-2 **87190-80-5** 87190-84-9 87418-35-7 92562-88-4, 3'-Fluoro-2',3'-dideoxyguanosine 93014-16-5, 4-(2-Methyl-4-phenyl-5-oxazolyl)benzenesulfonamide 105380-83-4, 3'-Azido-2',3'-dideoxy-5-ethyluridine 105784-82-5, 3'-Azido-2',3'-dideoxy-5-bromouridine 106060-85-9 **107036-62-4**, 5'-Fluoro-2',3'-dideoxycytidine 107550-73-2 108441-50-5 108441-51-6, 3'-Azido-5-chloro-2',3'-dideoxyuridine 108895-46-1 109881-25-6 110142-99-9 110143-10-7 111495-90-0 111495-95-5 111495-96-6 111495-98-8 111496-01-6 114551-78-9 114753-53-6 115249-86-0, 2',3'-Dideoxy-3'-fluoro-5-bromouridine 115913-79-6 116333-41-6 119555-47-4 119644-22-3, 2',3'-Dideoxy-3'-fluoro-5-chlorouridine 119644-23-4 120443-30-3 120503-30-2, 6-Dimethylaminopurine-2',3'-dideoxyriboside 120503-34-6 120503-35-7, N-Ethyl-2',3'-dideoxyadenosine 120826-45-1 121117-72-4 121135-52-2 121135-53-3 121353-93-3 123027-56-5 123663-49-0 124770-85-0 124903-20-4 125056-58-8 126062-18-8 126320-77-2 126347-69-1 127245-22-1 **127492-31-3 127492-32-4** 129618-40-2 130108-72-4 130108-73-5, 4'-Azido-2'-deoxyadenosine 130108-74-6, 4'-Azido-2'-deoxyguanosine 130108-75-7, 4'-Azido-2'-deoxyuridine 130108-76-8, 4'-Azido-2'-deoxycytidine 130108-77-9, 4'-Azido-2'-deoxyinosine 130108-82-6, 4'-Azido-3'-deoxythymidine 130797-04-5 131293-25-9 131613-15-5 132235-73-5 132774-45-9 132796-66-8 132796-67-9 132796-68-0 132970-02-6 134379-77-4 134678-17-4, Efavir 135212-57-6 135525-66-5 135525-77-8 135560-41-7 135812-04-3 135812-34-9 136160-29-7 136160-30-0 136470-78-5, Ziagen 136816-75-6 136816-76-7 136816-96-1 136817-66-8 136891-12-8 137332-54-8 137945-48-3 138192-33-3 138226-12-7 139226-28-1 139418-97-6, 4'-Azido-5-chloro-2'-deoxyuridine 139888-11-2, 4'-Cyanothymidine 141030-34-4 141030-55-9 141781-17-1 142102-79-2 143390-74-3 143491-57-0 143809-38-5 143809-39-6 144239-69-0 144433-06-7 145417-33-0 145514-01-8 145986-26-1 146739-86-8 **147058-39-7** 147362-57-0 147440-15-1 147584-54-1 147920-12-5 147920-13-6 147920-19-2 148311-89-1 148472-83-7, 5-Chloro-3-(phenylsulfonyl)indole-2-carboxamide 149485-30-3 149485-98-3 149950-60-7 149950-61-8 150378-17-9, Indinavir 153562-59-5 153815-93-1 154598-52-4 158959-32-1, 1-[2-(4-Fluorophenyl)cyclopenten-1-yl]-4-(methylsulfonyl)benzene 158959-33-2, 1-[2-(4-Fluoro-2-methylphenyl)cyclopenten-1-yl]-4-(methylsulfonyl)benzene 158959-34-3, 1-[2-(4-Chlorophenyl)cyclopenten-1-yl]-4-(methylsulfonyl)benzene 158959-35-4, 1-[2-(2,4-Dichlorophenyl)cyclopenten-1-yl]-4-(methylsulfonyl)benzene 158959-37-6, 1-[2-(4-Trifluoromethylphenyl)cyclopenten-1-yl]-4-(methylsulfonyl)benzene 158959-42-3, 1-[2-(4-Methylthiophenyl)cyclopenten-1-yl]-4-(methylsulfonyl)benzene 158959-43-4, 1-[2-(4-Fluorophenyl)-4,4-dimethylcyclopenten-1-yl]-4-(methylsulfonyl)benzene 158959-46-7, 4-[2-(4-Fluorophenyl)cyclopenten-1-yl]benzenesulfonamide 158959-47-8,

4-[2-(4-Chlorophenyl)cyclopenten-1-yl]benzenesulfonamide 158959-56-9,
 4-[2-(4-Fluorophenyl)-4,4-dimethylcyclopenten-1-yl]benzenesulfonamide
 159429-69-3, 1-[2-(4-Methoxyphenyl)cyclopenten-1-yl]-4-
 (methylsulfonyl)benzene 159429-70-6, 1-[2-(4-Chlorophenyl)-4,4-
 dimethylcyclopenten-1-yl]-4-(methylsulfonyl)benzene 159499-99-7
 159519-65-0, Enfuvirtide 159989-64-7, Nelfinavir 160705-95-3
 160707-69-7 160707-70-0 160707-71-1 160963-01-9 162011-90-7
 162054-19-5 163303-19-3 163303-25-1 163303-29-5 163303-38-6
 163303-55-7 163451-80-7 165251-89-8 165328-42-7,
 1-[2-(2,3-Difluorophenyl)cyclopenten-1-yl]-4-(methylsulfonyl)benzene
 165328-49-4, 4-[2-(4-Chlorophenyl)-4,4-dimethylcyclopenten-1-
 yl]benzenesulfonamide 165328-51-8 168146-84-7 168299-83-0
 168299-90-9 168433-84-9 169154-04-5 169154-07-8 169154-19-2
 169154-24-9 169590-41-4, 4-[[5-(3-Fluoro-4-methoxyphenyl)-3-
 difluoromethyl]-1H-pyrazol-1-yl]benzenesulfonamide 169590-42-5
 169902-71-0, 4-[2-(3-Chloro-4-fluorophenyl)cyclopenten-1-
 yl]benzenesulfonamide 169902-74-3, 4-[2-(3-Fluoro-4-
 methoxyphenyl)cyclopenten-1-yl]benzenesulfonamide 169902-75-4,
 1-[2-(3-Chloro-4-methoxyphenyl)cyclopenten-1-yl]-4-(methylsulfonyl)benzene
 169951-23-9 169951-24-0 169951-25-1 169951-27-3 169951-28-4
 170569-31-0 170569-42-3 170569-50-3 170569-86-5,
 4-[5-(4-Chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-
 yl]benzenesulfonamide 170569-87-6, 4-[5-Phenyl-3-(trifluoromethyl)-1H-
 pyrazol-1-yl]benzenesulfonamide 170569-88-7, 4-[5-(4-Fluorophenyl)-3-
 (trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide 170569-91-2,
 4-[5-(4-Methoxyphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-
 yl]benzenesulfonamide 170570-05-5 170570-25-9 170570-29-3
 170570-31-7 170570-32-8 170570-33-9 170571-71-8 171888-46-3
 173776-67-5 174470-77-0 175676-91-2 175676-92-3 175677-05-1
 175677-06-2 175677-07-3 175677-13-1

RL: **PAC (Pharmacological activity); THU (Therapeutic use);** BIOL (Biological study); USES (Uses)

(methods and compns. for treatment or prevention of HIV infection and
 related conditions using cyclooxygenase-2 selective inhibitors and
antiviral agents)

IT 175677-14-2 175883-05-3 175883-36-0 177560-19-9 177560-23-5
 177560-29-1 177560-30-4 177560-34-8 177560-36-0 177560-38-2
 177560-61-1 177577-60-5 177660-54-7 177660-55-8 177660-56-9
 177660-67-2 177660-72-9 177660-73-0 177660-76-3 177660-77-4
 177660-78-5 177660-80-9, 2-Methyl-5-[1-[4-(methylsulfonyl)phenyl]-4-
 trifluoromethyl-1H-imidazol-2-yl]pyridine 177660-81-0 177660-85-4
 177660-89-8 177660-92-3, 4-[2-(5-Methylpyridin-3-yl)-4-(trifluoromethyl)-
 1H-imidazol-1-yl]benzenesulfonamide 177660-94-5 177661-00-6
 177661-01-7 177661-04-0 177661-06-2 177661-15-3 177661-17-5
 177661-18-6 177661-19-7 177661-49-3 177662-22-5 177754-42-6
 178870-32-1 178979-85-6 179382-91-3 180048-35-5 180302-52-7
 181377-89-9 181377-90-2 181627-94-1 181627-96-3 181627-98-5
 181628-00-2 181695-72-7 181695-81-8 181695-85-2 181696-18-4
 181696-33-3 181809-58-5 181809-60-9 181809-63-2 183136-88-1
 183610-65-3 185344-55-2 186804-50-2 186804-93-3,
 4-[2-(2-Methylpyridin-5-yl)cyclopenten-1-yl]benzenesulfonamide
 198470-84-7 201341-05-1 202138-50-9, Viread 202409-33-4
 202409-52-7 204864-54-0 214287-88-4 215122-07-9 215122-12-6
 215122-14-8 215122-18-2 215122-19-3 215122-20-6 215122-22-8
 215122-24-0 215122-27-3 215122-28-4 215122-29-5 215122-30-8
 215122-31-9 215122-32-0 215122-33-1 215122-35-3 215122-36-4
 215122-37-5 215122-38-6 215122-39-7 215122-43-3 215122-44-4
 215122-45-5 215122-46-6 215122-48-8 215122-49-9 215122-50-2
 215122-51-3 215122-52-4 215122-53-5 215122-55-7 215122-56-8

215122-58-0 215122-59-1 215122-60-4 215122-61-5 215122-62-6
215122-63-7 215122-65-9 215122-70-6 215122-71-7 215122-74-0
215122-75-1 215122-76-2 215122-77-3 215123-03-8 215123-07-2
215123-08-3 215123-16-3 215123-48-1 215123-52-7 215123-60-7
215123-61-8, 6,8-Dichloro-2-trifluoromethyl-2H-1-benzothiopyran-3-
carboxylic acid 215123-64-1 215123-70-9 215123-77-6 215123-79-8
215123-80-1 215123-84-5 220991-20-8 264878-87-7 266320-83-6
467427-54-9 468067-63-2 477594-33-5 477594-34-6 631912-94-2
639785-67-4 725250-87-3 725250-88-4 834911-85-2 834911-86-3
834911-87-4 834911-88-5 834911-90-9 834911-91-0

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(methods and compns. for treatment or prevention of HIV infection and
related conditions using cyclooxygenase-2 selective inhibitors and
antiviral agents)

IT 87190-80-5 107036-62-4, 5-Fluoro-2',3'-dideoxycytidine
127492-31-3 127492-32-4 147058-39-7

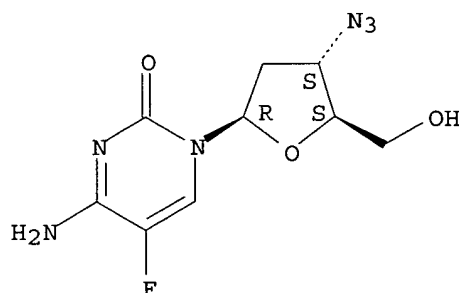
RL: PAC (**Pharmacological activity**); THU (**Therapeutic
use**); BIOL (Biological study); USES (Uses)

(methods and compns. for treatment or prevention of HIV infection and
related conditions using cyclooxygenase-2 selective inhibitors and
antiviral agents)

RN 87190-80-5 HCAPLUS

CN Cytidine, 3'-azido-2',3'-dideoxy-5-fluoro- (9CI) (CA INDEX NAME)

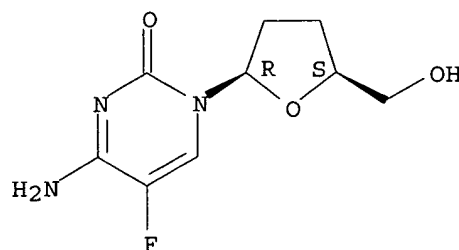
Absolute stereochemistry.



RN 107036-62-4 HCAPLUS

CN Cytidine, 2',3'-dideoxy-5-fluoro- (9CI) (CA INDEX NAME)

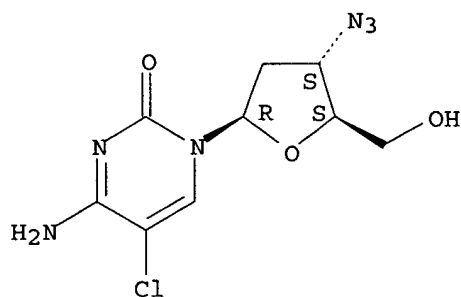
Absolute stereochemistry.



RN 127492-31-3 HCAPLUS

CN Cytidine, 3'-azido-5-chloro-2',3'-dideoxy- (9CI) (CA INDEX NAME)

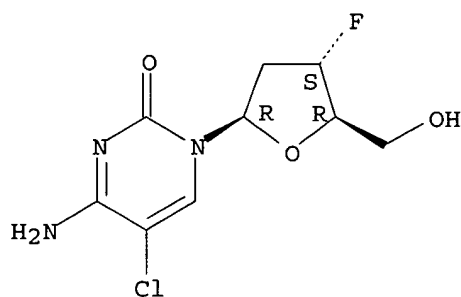
Absolute stereochemistry.



RN 127492-32-4 HCAPLUS

CN Cytidine, 5-chloro-2',3'-dideoxy-3'-fluoro- (9CI) (CA INDEX NAME)

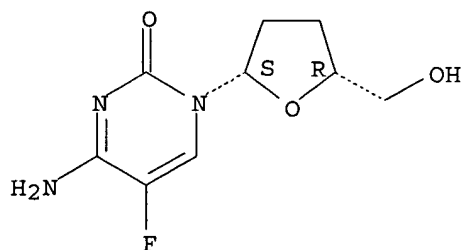
Absolute stereochemistry.



RN 147058-39-7 HCAPLUS

CN 2 (1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



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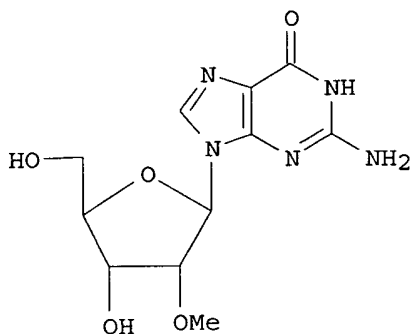
ACCESSION NUMBER: 2005:85160 HCAPLUS

DOCUMENT NUMBER: 142:355503

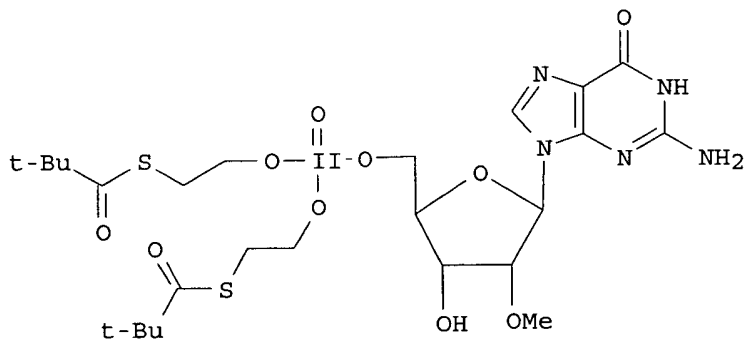
TITLE: Synthesis and Evaluation of S-Acyl-2-thioethyl Esters of Modified Nucleoside 5'-Monophosphates as Inhibitors of *Hepatitis C Virus* RNA Replication

AUTHOR(S): Prakash, Thazha P.; Prhavc, Marija; Eldrup, Anne B.;

Cook, P. Dan; Carroll, Steven S.; Olsen, David B.;
Stahlhut, Mark W.; Tomassini, Joanne E.; MacCoss,
Malcolm; Galloway, Sheila M.; Hilliard, Catherine;
Bhat, Balkrishen
CORPORATE SOURCE: Department of Medicinal Chemistry, ISIS
Pharmaceuticals, Carlsbad, CA, 92008, USA
SOURCE: Journal of Medicinal Chemistry (2005), 48(4),
1199-1210
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
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OTHER SOURCE(S): CASREACT 142:355503
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I



II

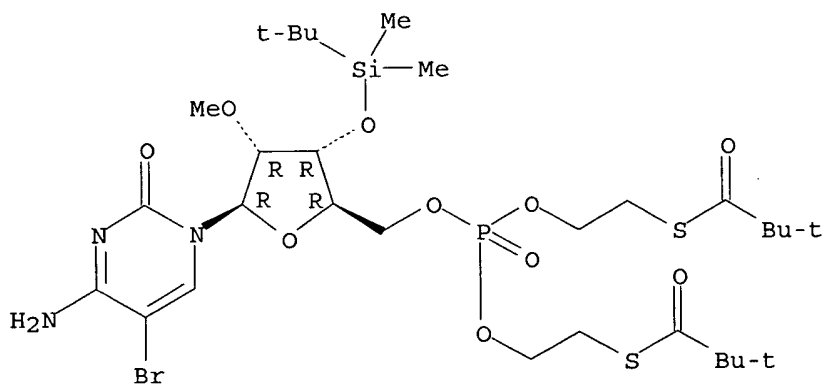
AB Several triphosphates of modified nucleosides, e.g. I, were identified as inhibitors ($IC_{50} = 0.08-3.8 \mu M$) of **hepatitis C virus** RNA-dependent RNA polymerase (RdRp). Although the initial SAR developed by determining the ability of the triphosphates to inhibit the in vitro activity of the **HCV** RdRp identified several potent inhibitors, none of the corresponding nucleosides exhibited significant inhibitory potency in a cell-based replicon assay. To improve upon the activity, bis(tBu-S-acyl-2-thioethyl) nucleoside 5'-monophosphate esters, e.g. II, were synthesized, and these derivs. exhibited improved potency compared to the corresponding nucleosides in the cell-based assay. Anal. of the intracellular metabolism demonstrated that the S-acyl-2-thioethyl (SATE) prodrug is metabolized to the 5'-triphosphate 40- to 155-fold more efficiently compared to the corresponding nucleoside. The prodrug

approach involving bis(tBuSATE)CMP ester significantly reduced the deamination of cytidine derivs. by cellular deaminases. Addnl., chromosomal aberration studies with the SATE prodrug in cells showed no statistically relevant increase in aberrations compared to the concurrent controls. The triphosphates of modified nucleosides were screened against the purified **HCV** RdRp for their ability to inhibit **HCV** NS5B mediated RNA synthesis. The replicon data indicated that none of the modified nucleosides, e.g. I, demonstrated significant activity in the cell-based assay, with EC50 values ranging from 20 to >50 μ M, in contrast to their corresponding nucleoside triphosphates that proved to be submicromolar to low micromolar (IC50 = 0.08-3.8 μ M) inhibitors of **HCV** NS5B mediated RNA synthesis.

- CC 33-9 (Carbohydrates)
Section cross-reference(s): 1, 7
- ST deaminase inhibitor nucleoside nucleotide synthesis **antiviral**
acylthioethyl ester human; **antiviral** nucleotide synthesis
prodrug deamination cellular deaminase chromosomal aberration; nucleoside
nucleotide synthesis **hepatitis C virus** RNA
replication inhibitor
- IT Drug delivery systems
(prodrugs; synthesis and evaluation of S-Acyl-2-thioethyl esters of
modified nucleoside 5'-monophosphates as inhibitors of
hepatitis C virus RNA replication)
- IT **Antiviral** agents
DNA replication
Deamination
Hepatitis C virus
Human
(synthesis and evaluation of S-Acyl-2-thioethyl esters of modified
nucleoside 5'-monophosphates as inhibitors of **hepatitis**
C virus RNA replication)
- IT Nucleosides, preparation
Nucleotides, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL
(Biological study); PREP (Preparation)
(synthesis and evaluation of S-Acyl-2-thioethyl esters of modified
nucleoside 5'-monophosphates as inhibitors of **hepatitis**
C virus RNA replication)
- IT Infection
(**viral**; synthesis and evaluation of S-Acyl-2-thioethyl esters
of modified nucleoside 5'-monophosphates as inhibitors of
hepatitis C virus RNA replication)
- IT 9025-06-3, Cytidine deaminase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(synthesis and evaluation of S-Acyl-2-thioethyl esters of modified
nucleoside 5'-monophosphates as inhibitors of **hepatitis**
C virus RNA replication)
- IT 2140-71-8 2140-72-9 3608-58-0 7057-33-2
RL: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological
study); RACT (Reactant or reagent)
(synthesis and evaluation of S-Acyl-2-thioethyl esters of modified
nucleoside 5'-monophosphates as inhibitors of **hepatitis**
C virus RNA replication)
- IT 444018-79-5P 444018-81-9P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant
or reagent)
(synthesis and evaluation of S-Acyl-2-thioethyl esters of modified
nucleoside 5'-monophosphates as inhibitors of **hepatitis**

C virus RNA replication)
IT 444019-15-2P 444019-17-4P 444019-19-6P 444019-23-2P 444019-27-6P
848860-67-3P **848860-94-6P**
RL: **PAC (Pharmacological activity)**; SPN (Synthetic preparation);
BIOL (Biological study); PREP (Preparation)
(synthesis and evaluation of S-Acyl-2-thioethyl esters of modified
nucleoside 5'-monophosphates as inhibitors of **hepatitis**
C virus RNA replication)
IT 14470-28-1, p-Anisylchlorodiphenylmethane 68703-51-5 84955-31-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and evaluation of S-Acyl-2-thioethyl esters of modified
nucleoside 5'-monophosphates as inhibitors of **hepatitis**
C virus RNA replication)
IT 120401-36-7P 161110-12-9P 168777-55-7P 367511-42-0P 444018-80-8P
444018-82-0P 444019-11-8P 444019-16-3P 444019-18-5P 444019-20-9P
444019-24-3P 444019-26-5P 444019-28-7P 632367-76-1P 848860-77-5P
848860-79-7P 848860-83-3P 848860-85-5P 848860-93-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(synthesis and evaluation of S-Acyl-2-thioethyl esters of modified
nucleoside 5'-monophosphates as inhibitors of **hepatitis**
C virus RNA replication)
IT **848860-94-6P**
RL: **PAC (Pharmacological activity)**; SPN (Synthetic preparation);
BIOL (Biological study); PREP (Preparation)
(synthesis and evaluation of S-Acyl-2-thioethyl esters of modified
nucleoside 5'-monophosphates as inhibitors of **hepatitis**
C virus RNA replication)
RN 848860-94-6 HCAPLUS
CN 5'-Cytidylic acid, 5-bromo-3'-O-[(1,1-dimethylethyl)dimethylsilyl]-2'-O-
methyl-, bis[2-[(2,2-dimethyl-1-oxopropyl)thio]ethyl] ester (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

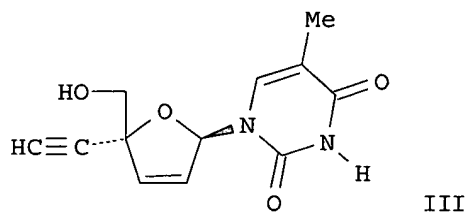
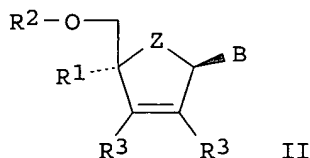
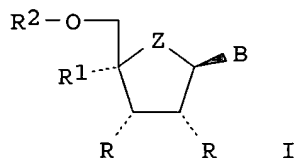


REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 6 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:701799 HCAPLUS
DOCUMENT NUMBER: 141:225774
TITLE: Preparation of 2',3'-dideoxy and 2',3'-dideohydro
nucleoside analogs as prodrugs for treating

viral infections, most notably HIV
INVENTOR(S): Cheng, Yung-chi; Tanaka, Hiromichi; Baba, Masanori
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 45 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004167096	A1	20040826	US 2004-781305	20040218
AU 2004260630	A1	20050210	AU 2004-260630	20040218
CA 2514466	AA	20050210	CA 2004-2514466	20040218
WO 2005011709	A1	20050210	WO 2004-US4713	20040218
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
BR 2004007374	A	20060110	BR 2004-7374	20040218
EP 1653976	A1	20060510	EP 2004-775776	20040218
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
CN 1777432	A	20060524	CN 2004-80010529	20040218
PRIORITY APPLN. INFO.:			US 2003-448554P	P 20030219
			WO 2004-US4713	W 20040218
OTHER SOURCE(S):	CASREACT 141:225774; MARPAT 141:225774			
GI				



AB Nucleosides I, wherein B is nucleobase; Z is O or CH₂; R is H, OH, halo, alkyl substituents; R1 can be H, Me, alkenyl, alkynyl; R2 is H, acyl, alkyl, ether, phosphoethers; and 2',3'-didehydro nucleosides II where Z is O; and R3 can alkyl, alkenyl, alkynyl, halo, hydroxy, were prepared as

prodrugs and **antiviral** agents. Thus, the synthesized 2',3'-dideoxy and didehydro nucleoside analogs were tested as potential **antiviral**, anti-HIV and anti-infective prodrugs as independent agents, or in combination with other agents. Specifically, didehydro nucleoside III was prepared and tested in vitro as potent anti-HIV-1 agent ($EC_{50} = 0.25 \pm 0.14$) and as well less toxic ($ID_{50} > 256$) as D4T, therefor has the potential as a new anti-HIV drug.

- IC ICM A61K031-7076
ICS A61K031-7072; A61K031-522; A61K031-675
- INCL 514046000; 514047000; 514050000; 514081000; 514263340; 514263370;
514269000; 536026100; 536027600; 536028530
- CC 33-9 (Carbohydrates)
Section cross-reference(s): 1, 63
- ST deoxy nucleoside analog prepn **antiviral** prodrug human; HIV
prodrug deoxy nucleoside analog prepn; combination chemotherapy deoxy
nucleoside analog prodrug prepn; dehydro nucleoside analog prepn
antiviral prodrug
- IT Nucleosides, preparation
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN
(Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
PREP (Preparation); USES (Uses)
(dideoxy, unsatd.; synthesis of 2',3'-dideoxy and didehydro nucleoside
analogs and their evaluation as **antiviral**, anti-HIV and
anti-infective prodrugs)
- IT Nucleosides, preparation
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN
(Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
PREP (Preparation); USES (Uses)
(dideoxy; synthesis of 2',3'-dideoxy and didehydro nucleoside analogs
and their evaluation as **antiviral**, anti-HIV and
anti-infective prodrugs)
- IT Drug delivery systems
(prodrugs; synthesis of 2',3'-dideoxy and didehydro nucleoside analogs
and their evaluation as **antiviral**, anti-HIV and
anti-infective prodrugs)
- IT Nucleoside analogs
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN
(Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
PREP (Preparation); USES (Uses)
(synthesis of 2',3'-dideoxy and didehydro nucleoside analog and their
evaluation as **antiviral**, anti-HIV and anti-infective
prodrugs)
- IT Anti-AIDS agents
Antiviral agents
Combination chemotherapy
(synthesis of 2',3'-dideoxy and didehydro nucleoside analogs and their
evaluation as **antiviral**, anti-HIV and anti-infective
prodrugs)
- IT Adenoviridae
Cytomegalovirus
Dengue virus
Flavivirus
Hepatitis B virus
Hepatitis C virus
Human
Human T-lymphotropic virus 1
Human T-lymphotropic virus 2
Human herpesvirus 1
Human herpesvirus 2

Human herpesvirus 3
 Human herpesvirus 4
 Human herpesvirus 8
 Human immunodeficiency virus 1
 Human immunodeficiency virus 2
 Human papillomavirus
 Japanese encephalitis virus
 Rous sarcoma virus
 West Nile virus
 Yellow fever virus

(virus tested against 2',3'-dideoxy and didehydro nucleoside analogs)

IT 634907-28-1P

RL: BYP (Byproduct); IMF (Industrial manufacture); PREP (Preparation)
 (synthesis of 2',3'-dideoxy and didehydro nucleoside analog and their
 evaluation as **antiviral**, anti-HIV and anti-infective
 prodrugs)

IT 3056-17-5P, d4T 151989-82-1P 634907-29-2P 634907-30-5P
 717913-88-7P 717913-89-8P 717913-90-1P 717913-91-2P 744217-09-2P
 RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN
 (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
 PREP (Preparation); USES (Uses)

(synthesis of 2',3'-dideoxy and didehydro nucleoside analog and their
 evaluation as **antiviral**, anti-HIV and anti-infective
 prodrugs)

IT 52523-37-2P 128070-96-2P 128093-86-7P 135911-57-8P 499970-82-0P
 512184-16-6P 512184-17-7P 634907-27-0P 744217-10-5P 744217-11-6P
 744217-12-7P 744217-13-8P 744217-14-9P 744217-15-0P 744217-16-1P
 744217-17-2P 744217-20-7P 744217-21-8P 744217-22-9P 744217-23-0P
 744217-25-2P 744217-26-3P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic
 preparation); PREP (Preparation); RACT (Reactant or reagent)
 (synthesis of 2',3'-dideoxy and didehydro nucleoside analog and their
 evaluation as **antiviral**, anti-HIV and anti-infective
 prodrugs)

IT 61-33-6D, derivative 4097-22-7, Adenosine, 2',3'-dideoxy- 7481-89-2, DdC
 30516-87-1, AZT 59492-11-4 69655-05-6, DdI 107036-62-4
 126456-36-8, L 685434 127749-96-6 127779-20-8, Saquinavir
 129467-48-7 129467-49-8 129618-40-2, Nevirapine 134379-77-4
 134678-17-4, 3TC 136470-78-5, Abacavir 136817-59-9, Delavirdine
 138483-63-3, L 689502 138483-77-9 138483-78-0 138498-62-1
 140196-60-7, p9941 141804-42-4, KNI 174 142340-99-6, Adefovir
 dipivoxil 143224-34-4, Telinavir 143491-54-7, FTC 144141-97-9,
 A-80987 144779-91-9, r-87366 145631-07-8 147058-39-7
 147384-69-8, KNI 227 149267-24-3, CGP 53820 149845-06-7, Saquinavir
 mesylate 150378-17-9, Indinavir 151867-81-1, XM323 154598-52-4,
 Efavirenz 154612-39-2, Palinavir 154612-58-5 155213-67-5, Ritonavir
 159519-65-0 159929-71-2 159989-64-7, Nelfinavir 160231-42-5,
 VB-11328 161814-49-9, Agenerase 164514-52-7, Sdz pri 053
 173261-21-7, A 98881 174484-41-4, Tipranavir 175385-62-3, Lasinavir
 181785-84-2 183854-24-2, Sd 146 188762-00-7, A 83962 192725-17-0
 198904-31-3, Atazanavir 201341-05-1, Tenofovir disoproxil 744217-27-4
 744217-28-5 744217-29-6

RL: PAC (Pharmacological activity); THU (Therapeutic
 use); BIOL (Biological study); USES (Uses)
 (synthesis of 2',3'-dideoxy and didehydro nucleoside analog and their
 evaluation as **antiviral**, anti-HIV and anti-infective
 prodrugs)

IT 14046-57-2 94892-66-7 744217-18-3 744217-19-4 744217-24-1

RL: RCT (Reactant); RACT (Reactant or reagent)

(synthesis of 2',3'-dideoxy and didehydro nucleoside analog and their evaluation as **antiviral**, anti-HIV and anti-infective prodrugs)

IT 4330-20-5 61114-30-5

RL: RCT (Reactant); RACT (Reactant or reagent)

(synthesis of 2',3'-dideoxy and didehydro nucleoside analogs and their evaluation as **antiviral**, anti-HIV and anti-infective prodrugs)

IT 744217-30-9P 744217-31-0P 744217-32-1P 744217-33-2P 744217-34-3P
744217-35-4P 744217-36-5P 744217-37-6P 744217-38-7P 744217-39-8P
744217-40-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of 2',3'-dideoxy and didehydro nucleoside analogs and their evaluation as **antiviral**, anti-HIV and anti-infective prodrugs)

IT 107036-62-4 147058-39-7

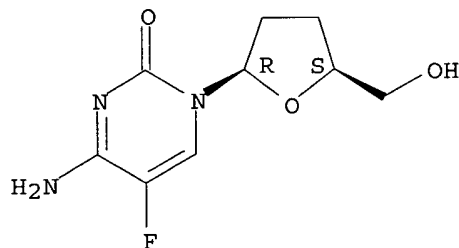
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(synthesis of 2',3'-dideoxy and didehydro nucleoside analog and their evaluation as **antiviral**, anti-HIV and anti-infective prodrugs)

RN 107036-62-4 HCAPLUS

CN Cytidine, 2',3'-dideoxy-5-fluoro- (9CI) (CA INDEX NAME)

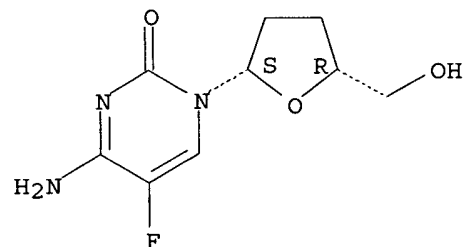
Absolute stereochemistry.



RN 147058-39-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L34 ANSWER 7 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:490275 HCAPLUS

DOCUMENT NUMBER: 141:59691

TITLE: Systemic delivery of **antiviral** agents
INVENTOR(S): Ashton, Paul; Chen, Jianbing; Smith, Thomas J.
PATENT ASSIGNEE(S): Control Delivery Systems, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 37 pp., Cont.-in-part of U.S.
Ser. No. 96,877.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004115268	A1	20040617	US 2003-713336	20031113
US 6375972	B1	20020423	US 2000-558207	20000426
US 2002102307	A1	20020801	US 2002-96877	20020314
US 2005186279	A1	20050825	US 2005-81142	20050315
PRIORITY APPLN. INFO.:			US 2000-558207	A1 20000426
			US 2002-96877	A2 20020314
			US 2002-425943P	P 20021113

AB The systems and methods disclosed herein provide sustained delivery of a therapeutic agent for treating a patient, e.g., human, to obtain a desired local or systemic physiol. or pharmacol. effect. Method includes positioning the sustained released drug delivery system at an area wherein release of the agent is desired and allowing the agent to pass through the device to the desired area of treatment. In some embodiments, the method is for treating or reducing the risk of retroviral or lentiviral infection. In certain embodiments, the method is for preventing or reducing the risk of mother-to-child transmission of HIV, wherein the therapeutic agent is an **antiviral** agent.

IC ICM A61K009-24

INCL 424473000

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1, 15

ST sustained delivery **antiviral**

IT Polysiloxanes, biological studies

RL: TEM (Technical or engineered material use); THU (Therapeutic use);

BIOL (Biological study); USES (Uses)

(-carbonate copolymer; systemic delivery of **antiviral** agents)

IT **Hepatitis**

(C; systemic delivery of **antiviral** agents)

IT Infection

Reproductive system, neoplasm

(acuminate wart; systemic delivery of **antiviral** agents)

IT Wart

(acuminate, genital; systemic delivery of **antiviral** agents)

IT Wart

(acuminate, vulvar; systemic delivery of **antiviral** agents)

IT Development, mammalian postnatal

(child; systemic delivery of **antiviral** agents)

IT Gelatins, biological studies

RL: TEM (Technical or engineered material use); THU (Therapeutic use);

BIOL (Biological study); USES (Uses)

(crosslinked; systemic delivery of **antiviral** agents)

IT Infection

(dengue; systemic delivery of **antiviral** agents)

IT Wart

(epidermodysplasia verruciformis; systemic delivery of **antiviral** agents)

IT Infection
(foot-and-mouth disease; systemic delivery of **antiviral** agents)

IT Polyvinyl acetals
RL: TEM (Technical or engineered material use); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(formals; systemic delivery of **antiviral** agents)

IT Fever and Hyperthermia
(hemorrhagic, **viral**; systemic delivery of **antiviral** agents)

IT Infection
(**hepatitis C**; systemic delivery of **antiviral** agents)

IT Infection
(herpes zoster; systemic delivery of **antiviral** agents)

IT Coating materials
(impermeable; systemic delivery of **antiviral** agents)

IT Lentivirus
Retroviridae
(infection; systemic delivery of **antiviral** agents)

IT Polymers, biological studies
RL: TEM (Technical or engineered material use); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(microporous; systemic delivery of **antiviral** agents)

IT Wart
(nongenital; systemic delivery of **antiviral** agents)

IT Collagens, biological studies
RL: TEM (Technical or engineered material use); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(polyanion modified insol.; systemic delivery of **antiviral** agents)

IT Drug delivery systems
(polymer-bound; systemic delivery of **antiviral** agents)

IT Anions
Cations
(polyvalent, modified insol. collagen; systemic delivery of **antiviral** agents)

IT Drug delivery systems
(prodrugs; systemic delivery of **antiviral** agents)

IT Polyamides, biological studies
RL: TEM (Technical or engineered material use); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(soft; systemic delivery of **antiviral** agents)

IT Drug delivery systems
(sustained-release; systemic delivery of **antiviral** agents)

IT AIDS (disease)
Anti-AIDS agents
Antiviral agents
Blood plasma
Cowpox virus
Enterovirus
Erythema
Human
Human herpesvirus
Human herpesvirus 6
Human herpesvirus 8
Human immunodeficiency virus
Human immunodeficiency virus 1
Measles virus

Membranes, nonbiological
Molluscum contagiosum virus
Monkeypox virus
Pseudocowpox virus
Rubella
 (systemic delivery of **antiviral** agents)

IT Interferons
Interleukins
Trichosanthin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (systemic delivery of **antiviral** agents)

IT Ethylene-propylene rubber
RL: TEM (Technical or engineered material use); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
 (systemic delivery of **antiviral** agents)

IT Fluoropolymers, biological studies
RL: TEM (Technical or engineered material use); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
 (systemic delivery of **antiviral** agents)

IT Natural rubber, biological studies
RL: TEM (Technical or engineered material use); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
 (systemic delivery of **antiviral** agents)

IT Polyamides, biological studies
RL: TEM (Technical or engineered material use); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
 (systemic delivery of **antiviral** agents)

IT Polycarbonates, biological studies
RL: TEM (Technical or engineered material use); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
 (systemic delivery of **antiviral** agents)

IT Polyesters, biological studies
RL: TEM (Technical or engineered material use); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
 (systemic delivery of **antiviral** agents)

IT Polyolefins
RL: TEM (Technical or engineered material use); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
 (systemic delivery of **antiviral** agents)

IT Polyurethanes, biological studies
RL: TEM (Technical or engineered material use); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
 (systemic delivery of **antiviral** agents)

IT Polyvinyl acetals
RL: TEM (Technical or engineered material use); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
 (systemic delivery of **antiviral** agents)

IT Silicone rubber, biological studies
RL: TEM (Technical or engineered material use); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
 (systemic delivery of **antiviral** agents)

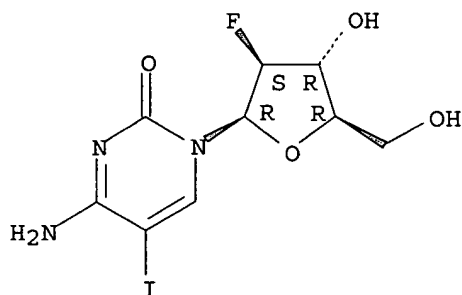
IT Infection
 (varicella; systemic delivery of **antiviral** agents)

IT Infection
 (variola; systemic delivery of **antiviral** agents)

IT Reproductive system, neoplasm
 (vulvar acuminate wart; systemic delivery of **antiviral**
 agents)

- IT 9002-89-5, Polyvinyl alcohol
RL: TEM (Technical or engineered material use); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(cross-linked; systemic delivery of **antiviral** agents)
- IT 9003-39-8, Polyvinylpyrrolidone
RL: TEM (Technical or engineered material use); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(crosslinked; systemic delivery of **antiviral** agents)
- IT 9010-79-1
RL: TEM (Technical or engineered material use); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(ethylene-propylene rubber, systemic delivery of **antiviral** agents)
- IT 100-33-4, Pentamidine 107-36-8 145-63-1, Suramin 147-94-4,
Cytarabine 548-04-9, Hypericin 768-94-5, Amantadine 1264-62-6,
Anamycin 3416-05-5, 2',3'-Dideoxythymidine 4097-22-7,
2',3'-Dideoxyadenosine 5536-17-4, Vidarabine 7481-89-2, Zalcitabine
13392-28-4, Rimantadine 30516-87-1, 3-Azido-3-deoxythymidine
36791-04-5, Ribavirin 39483-48-2 **69123-90-6**, Fiacitabine
69123-98-4, Fialuridine 69304-47-8 69655-05-6, Didanosine
72301-79-2, Enviroxime 74131-08-1, Uridine, 5-[(1E)-2-chloroethenyl]-2'-
deoxy- 75128-58-4, Deoxyacyclovir 84408-37-7, Desciclovir
85326-06-3, 2',3'-Dideoxyguanosine 110143-10-7, F-DdA 117525-25-4
119555-47-4 129618-40-2, Nevirapine 134678-17-4, 3TC 140459-12-7,
Fluorothymidine 530135-43-4, Foscarnet
RL: **PAC (Pharmacological activity); THU (Therapeutic use);** BIOL (Biological study); USES (Uses)
(systemic delivery of **antiviral** agents)
- IT 75-35-4, Vinylidene chloride, biological studies 107-13-1D,
Acrylonitrile, copolymer 9002-83-9, Polytrifluorochloroethylene
9002-84-0, Polytetrafluoroethylene 9002-85-1, Polyvinylidene chloride
9002-86-2, Polyvinyl chloride 9002-88-4, Polyethylene 9002-88-4D,
Polyethylene, chlorinated 9003-00-3, Vinyl chloride-acrylonitrile
copolymer 9003-17-2, Polybutadiene 9003-20-7 9003-27-4,
Polyisobutylene 9003-31-0, Polyisoprene 9003-63-8,
Polybutylmethacrylate 9003-77-4, Polyethyl hexylacrylate 9004-34-6,
Cellulose, biological studies 9004-34-6D, Cellulose, cross-linked,
biological studies 9004-36-8, Cellulose acetate butyrate 9004-38-0,
Cellulose acetate phthalate 9004-39-1, Cellulose acetate propionate
9010-86-0, Ethylene ethylacrylate copolymer 9011-06-7, Vinylidene
chloride-vinyl chloride copolymer 9011-14-7, Polymethylmethacrylate
9016-00-6, Poly[oxy(dimethylsilylene)] 24936-68-3, Poly(4,4'-
isopropylidene diphenylene carbonate), biological studies 24991-31-9,
Polyvinylbutyrate 24991-31-9D, Polyvinyl butyrate, cross-linked
25014-41-9, Polyacrylonitrile 25037-78-9, Ethylene vinylchloride
copolymer 25038-59-9, Polyethylene terephthalate, biological studies
30847-10-0, Vinyl chloride-diethyl fumarate copolymer
RL: TEM (Technical or engineered material use); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(systemic delivery of **antiviral** agents)
- IT **69123-90-6**, Fiacitabine
RL: **PAC (Pharmacological activity); THU (Therapeutic use);** BIOL (Biological study); USES (Uses)
(systemic delivery of **antiviral** agents)
- RN 69123-90-6 HCAPLUS
- CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy-2-fluoro- β -D-arabinofuranosyl)-
5-iodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L34 ANSWER 8 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:430732 HCAPLUS

DOCUMENT NUMBER: 140:428994

TITLE: Sustained release drug delivery system for
antiviral agents and methods for
antiviral therapy

INVENTOR(S): Ashton, Paul; Chen, Jianbing; Smith, Thomas J.

PATENT ASSIGNEE(S): Control Delivery Systems, Inc., USA

SOURCE: PCT Int. Appl., 85 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004043435	A2	20040527	WO 2003-US36637	20031113
WO 2004043435	A3	20040708		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003287666	A1	20040603	AU 2003-287666	20031113
PRIORITY APPLN. INFO.:			US 2002-425943P	P 20021113
			WO 2003-US36637	W 20031113

AB The systems and methods disclosed herein provide sustained delivery of a therapeutic agent for treating a patient, e.g., human, to obtain a desired local or systemic physiol. or pharmacol. effect. Method includes positioning the sustained-released drug delivery system at an area wherein release of the agent is desired and allowing the agent to pass through the device to the desired area of treatment. In some embodiments, the method is for treating or reducing the risk of retroviral or lentiviral infection. In certain embodiments, the method is for preventing or reducing the risk of mother-to-child transmission of HIV, wherein the therapeutic agent is an **antiviral** agent.

IC ICM A61K009-00

CC 63-5 (Pharmaceuticals)

ST sustained release drug delivery system implant **antiviral** agent
antiAIDS

IT **Hepatitis**
 (C; sustained-release drug delivery system for **antiviral**
 agents and methods for **antiviral** therapy)

IT Infection
 (acuminata of Buschke and Lowenstein; sustained-release drug delivery
 system for **antiviral** agents and methods for **antiviral**
 therapy)

IT Infection
 Reproductive system, neoplasm
 (acuminate wart, giant; sustained-release drug delivery system for
 antiviral agents and methods for **antiviral** therapy)

IT Wart
 (acuminate, genital, giant; sustained-release drug delivery system for
 antiviral agents and methods for **antiviral** therapy)

IT Wart
 (acuminate, vulvar, giant; sustained-release drug delivery system for
 antiviral agents and methods for **antiviral** therapy)

IT AIDS (disease)
 (childhood; sustained-release drug delivery system for
 antiviral agents and methods for **antiviral** therapy)

IT Polymers, biological studies
 RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (coating; sustained-release drug delivery system for **antiviral**
 agents and methods for **antiviral** therapy)

IT Gelatins, biological studies
 RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (crosslinked; sustained-release drug delivery system for
 antiviral agents and methods for **antiviral** therapy)

IT Infection
 (dengue; sustained-release drug delivery system for **antiviral**
 agents and methods for **antiviral** therapy)

IT Wart
 (epidermodysplasia verruciformis; sustained-release drug delivery
 system for **antiviral** agents and methods for **antiviral**
 therapy)

IT Erythema
 (fifth disease; sustained-release drug delivery system for
 antiviral agents and methods for **antiviral** therapy)

IT Polyvinyl acetals
 RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (formals; sustained-release drug delivery system for **antiviral**
 agents and methods for **antiviral** therapy)

IT Infection
 (hand-foot-and-mouth disease; sustained-release drug delivery system
 for **antiviral** agents and methods for **antiviral**
 therapy)

IT Fever and Hyperthermia
 (hemorrhagic, **viral**; sustained-release drug delivery system
 for **antiviral** agents and methods for **antiviral**
 therapy)

IT Infection
 (**hepatitis** C; sustained-release drug delivery system for
 antiviral agents and methods for **antiviral** therapy)

IT Infection

- (herpes zoster; sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT Films
(impermeable, of polymer coating; sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT Drug delivery systems
(implants, controlled-release; sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT Enterovirus
Human immunodeficiency virus 1
Lentivirus
Measles virus
Molluscum contagiosum virus
Monkeypox virus
Orf virus
Pseudocowpox virus
Retroviridae
(infection; sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT Collagens, uses
RL: NUU (Other use, unclassified); USES (Uses)
(insol., microporous polymer formed from; sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT Infection
(kaposi varicelliform eruption; sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT Infection
(measles; sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT Blood plasma
(modulate therapeutic agent concentration in; sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT Wart
(nongenital; sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT Polyamides, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(plasticized, soft; sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT Polyesters, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(plasticized; sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT Polysiloxanes, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polycarbonate-; sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT Vinyl compounds, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

- (polymers; sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT Polycarbonates, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polysiloxane-; sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT Drug delivery systems
(prodrugs; sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT Infection
(roseola infantum; sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT Anti-AIDS agents
Antiviral agents
Human herpesvirus
Human herpesvirus 6
Human immunodeficiency virus
Rubella
(sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT Ethylene-propylene rubber
Fluoropolymers, biological studies
Fluoropolymers, biological studies
Natural rubber, biological studies
Polycarbonates, biological studies
Polyesters, biological studies
Polyolefins
Polyoxyalkylenes, biological studies
Polyoxyalkylenes, biological studies
Polysiloxanes, biological studies
Polyurethanes, biological studies
Polyvinyl acetals
Silicone rubber, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT Interferons
Interleukins
Trichosanthin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT Drug delivery systems
(sustained-release; sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT Infection
(vaccinia, human; sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT Infection
(varicella; sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT Infection
(variola; sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT Infection
(**viral**, Bowenoid Papulosis; sustained-release drug delivery system for **antiviral** agents and methods for **antiviral**

- therapy)
- IT Reproductive system, neoplasm
(vulvar acuminate wart, giant; sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT 9010-79-1
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ethylene-propylene rubber, sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT 9004-34-6D, Cellulose, acylated, esterified
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(insol., nonerodible; sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT 9016-00-6, Poly[oxy(dimethylsilylene)]
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medical grade; sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT 75-01-4D, Vinylchloride, polymers 75-35-4, Vinylidene chloride, biological studies 557-04-0, Magnesium stearate, 9002-83-9, Polytrifluorochloroethylene 9002-84-0, Polytetrafluoroethylene 9002-85-1, Polyvinylidene chloride 9002-86-2, Polyvinylchloride 9002-86-2D, Polyvinyl chloride, plasticized 9002-88-4, Polyethylene 9002-88-4D, Polyethylene, chlorinated 9002-89-5D, Polyvinyl alcohol, cross-linked 9003-00-3, Vinyl chloride-acrylonitrile copolymer 9003-17-2, Polybutadiene 9003-20-7, Polyvinyl acetate 9003-27-4, Polyisobutylene 9003-31-0, Polyisoprene 9003-39-8D, Polyvinylpyrrolidone, cross-linked 9003-63-8, Polybutylmethacrylate 9003-77-4, Polyethyl hexylacrylate 9004-36-8, Cellulose acetatebutyrate 9004-38-0, Cellulose acetate phthalate 9004-39-1, Cellulose acetate propionate 9010-76-8 9010-86-0, Ethylene ethylacrylate copolymer 9011-06-7, Vinylidene chloride-vinyl chloride copolymer 9011-14-7, Polymethylmethacrylate 24936-68-3, biological studies 24937-78-8D, Ethylene vinylacetate copolymer, plasticized 24991-31-9, Polyvinylbutyrate 24991-31-9D, Polyvinylbutyrate, cross-linked 25014-41-9 25037-78-9, Ethylene vinylchloride copolymer 25038-59-9D, Polyethylene terephthalate, plasticized 25322-68-3, Polyethylene glycol 30847-10-0 84420-13-3
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sustained-release drug delivery system for **antiviral** agents and methods for **antiviral** therapy)
- IT 50-91-9, Floxuridine 54-42-2, Idoxuridine 70-00-8, Trifluorothymidine 100-33-4, Pentamidine 107-36-8 145-63-1, Suramin 147-94-4, Cytarabine 548-04-9, Hypericin 768-94-5, Amantadine 3056-17-5, Stavudine 3416-05-5, 2',3'-Dideoxythymidine 4097-22-7, 2',3'-Dideoxyadenosine 5536-17-4, Vidarabine 7481-89-2, Dideoxycytidine 13392-28-4, Rimantadine 15176-29-1, Edoxudine 19130-96-2, Deoxynojirimycin 30516-87-1, Zidovudine 36791-04-5, Ribavirin 59277-89-3, Acyclovir 63585-09-1 **69123-90-6**, Fiacitabine 69123-98-4, Fialuridine 69655-05-6, Dideoxyinosine 72301-79-2, Enviroxime 72559-06-9, Ansamycin 75128-58-4, Deoxyacyclovir 77530-02-0 82410-32-0, Ganciclovir 84408-37-7, Desciclovir 84472-85-5 85326-06-3, 2',3'-Dideoxyguanosine 110143-10-7 110143-10-7 117525-25-4 119555-47-4 121353-93-3 122757-54-4 122929-23-1 123774-72-1, Sargramostim 129618-40-2, Nevirapine 134678-17-4 134892-26-5 136817-59-9, Delavirdine

140459-12-7, Fluorothymidine 154598-52-4, Efavirenz 344427-81-2
530135-43-4, Foscarnet

RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(sustained-release drug delivery system for **antiviral** agents
and methods for **antiviral** therapy)

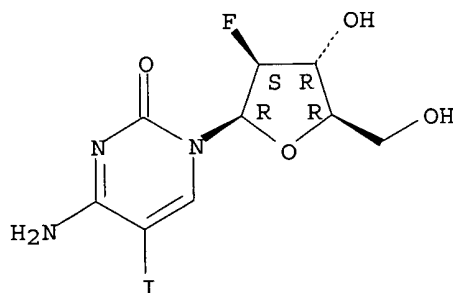
IT 69123-90-6, Fiacitabine

RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(sustained-release drug delivery system for **antiviral** agents
and methods for **antiviral** therapy)

RN 69123-90-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy-2-fluoro- β -D-arabinofuranosyl)-
5-iodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L34 ANSWER 9 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:428805 HCAPLUS

DOCUMENT NUMBER: 141:1201

TITLE: Modified nucleosides as **antiviral** agents

INVENTOR(S): Stuyver, Lieven J.; Chu, Chung K.

PATENT ASSIGNEE(S): Pharmasset, Ltd., USA; University of Georgia Research
Foundation, Inc.

SOURCE: PCT Int. Appl., 49 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004043402	A2	20040527	WO 2003-US36224	20031112
WO 2004043402	A3	20040805		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2003290816	A1	20040603	AU 2003-290816	20031112
US 2004157793	A1	20040812	US 2003-706865	20031112

PRIORITY APPLN. INFO.:

US 2002-425534P

P 20021112

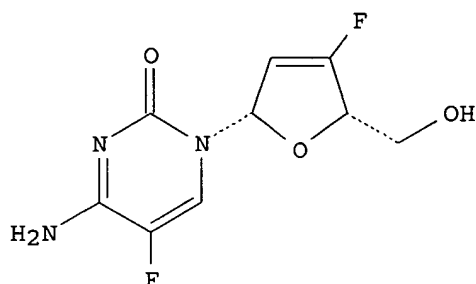
WO 2003-US36224

W 20031112

OTHER SOURCE(S):

MARPAT 141:1201

GI



AB The present invention relates to 3' substituted-2',3'-dideoxy- β -L-nucleosides and their pharmaceutically acceptable salts and prodrugs thereof, for the treatment of infectious viral diseases, in general, particularly HBV and HIV viral infections and more particularly, HBV and HIV viral infections that are resistant to other **antiviral** drugs. A number of compds. including I showed potent anti-HBV activities in HepAD38 cells.

IC ICM A61K

CC 1-5 (Pharmacology)

ST **antiviral** nucleoside

IT **Antiviral** agents

Hepatitis B virus

Human immunodeficiency virus

(modified nucleosides as **antiviral** agents)

IT Nucleosides, biological studies

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(modified nucleosides as **antiviral** agents)

IT Drug delivery systems

(prodrugs; modified nucleosides as **antiviral** agents)

IT 106941-25-7, Adefovir 134678-17-4, 3Tc 135212-57-6 137530-41-7,
(+)-FTC 143491-57-0, (-)-FTC 181623-96-1 181785-84-2 181785-91-1
221662-50-6 396653-01-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(modified nucleosides as **antiviral** agents)

IT 3424-98-4 40093-94-5 59277-89-3, Acyclovir **69123-90-6**

69304-47-8, BVDU 74886-33-2 77181-69-2 82410-32-0, Ganciclovir

92999-29-6 113852-35-0 113852-37-2, Cidofovir 142217-69-4, Entecavir

147127-20-6, Tenofovir 163252-36-6 207920-87-4

RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(modified nucleosides as **antiviral** agents)

IT **69123-90-6**

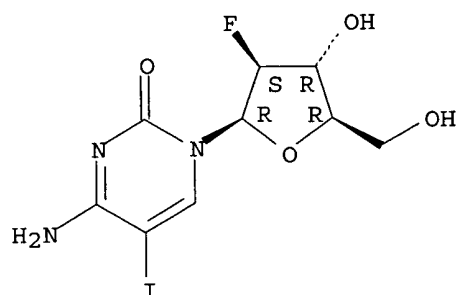
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(modified nucleosides as **antiviral** agents)

RN 69123-90-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy-2-fluoro- β -D-arabinofuranosyl)-
5-iodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L34 ANSWER 10 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:255259 HCAPLUS

DOCUMENT NUMBER: 141:325184

TITLE: **Antiviral** β -L-nucleosides specific for **hepatitis** B virus infection

AUTHOR(S): Bryant, Martin L.; Bridges, Edward G.; Placidi, Laurent; Faraj, Abdesslem; Loi, Anna-Giulia; Pierra, Claire; Benzaria, Samira; Dukhan, David; Gosselin, Gilles; Imbach, Jean-Louis; Hernandez, Brenda; Juodawlkis, Amy; Tennant, Bud; Korba, Brent; Cote, Paul; Cretton-Scott, Erika; Schinazi, Raymond F.; Myers, Maureen; Sommadossi, Jean-Pierre

CORPORATE SOURCE: Idenix, Inc., Cambridge, MA, 02140, USA
SOURCE: Frontiers in Viral Hepatitis (2003), 245-261.

Editor(s): Schinazi, Raymond F.; Sommadossi, Jean-Pierre; Rice, Charles M. Elsevier: Amsterdam, Neth.

CODEN: 69FEJF; ISBN: 0-444-50986-0

DOCUMENT TYPE: Conference

LANGUAGE: English

AB The authors describe β -L-nucleosides that specifically inhibits **hepatitis** B virus (HBV) replication, focusing on L-dA, L-dC, and L-dT, which are considered the most potent, selective and specific members of the class. It describes the structure-activity relationships of β -L-nucleosides and the **antiviral** specificity of L-dC, L-dT, and L-dC. The intracellular activation, metabolism, and pharmacol., pharmacokinetic profiles of these β -L-nucleosides, and their **antiviral** activity and safety in the woodchuck chronic **hepatitis** model are also discussed, as well as their selectivity and lack of cellular toxicity.

CC 1-5 (Pharmacology)

ST nucleoside analog **hepatitis** B virus **antiviral** agent

IT **Hepatitis**

(B; **antiviral** β -L-nucleosides specific for **hepatitis** B virus infection in relation to pharmacokinetics and toxicity)

IT **Antiviral** agents

Hepatitis B virus

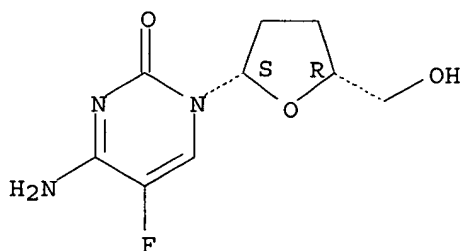
Human

Mitochondria

(**antiviral** β -L-nucleosides specific for **hepatitis** B virus infection in relation to pharmacokinetics and

- toxicity)
- IT Structure-activity relationship
(antiviral; antiviral β -L-nucleosides specific for hepatitis B virus infection in relation to pharmacokinetics and toxicity)
- IT Infection
(hepatitis B; antiviral β -L-nucleosides specific for hepatitis B virus infection in relation to pharmacokinetics and toxicity)
- IT 3424-98-4, NV 02B
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiviral β -L-nucleosides specific for hepatitis B virus infection in relation to pharmacokinetics and toxicity)
- IT 14365-45-8, NV 02A 40093-94-5, NV 02C
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiviral β -L-nucleosides specific for hepatitis B virus infection in relation to pharmacokinetics and toxicity)
- IT 61246-68-2 121154-51-6, β -L-2',3'-Dideoxycytidine 127501-59-1
128075-91-2 132979-39-6 134678-17-4 135212-56-5 135212-57-6
143491-57-0 144490-02-8 147058-39-7, β -L-2',3'-Dideoxy-5-fluorocytidine 160963-01-9 160963-15-5 177365-14-9
181785-84-2 182929-00-6 182929-01-7 186648-57-7 201295-39-8
216571-37-8 244097-84-5 265988-73-6 374107-79-6
381719-94-4 381719-95-5 381719-96-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiviral β -L-nucleosides specific for hepatitis B virus infection in relation to pharmacokinetics and toxicity)
- IT 147058-39-7, β -L-2',3'-Dideoxy-5-fluorocytidine
160963-15-5 265988-73-6 374107-79-6
381719-94-4 381719-95-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiviral β -L-nucleosides specific for hepatitis B virus infection in relation to pharmacokinetics and toxicity)
- RN 147058-39-7 HCAPLUS
- CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

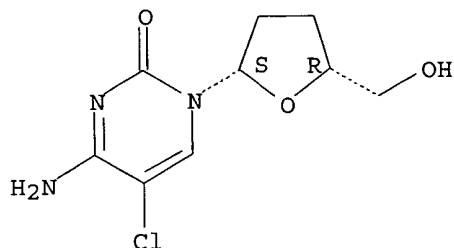
Absolute stereochemistry. Rotation (-).



RN 160963-15-5 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-chloro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

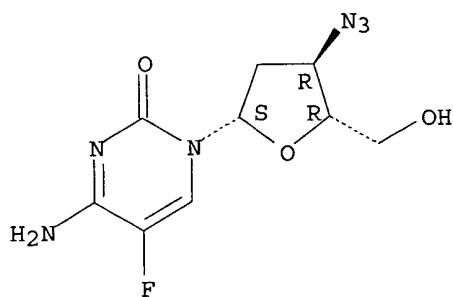
Absolute stereochemistry. Rotation (-).



RN 265988-73-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(3-azido-2,3-dideoxy-β-L-erythro-pentofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

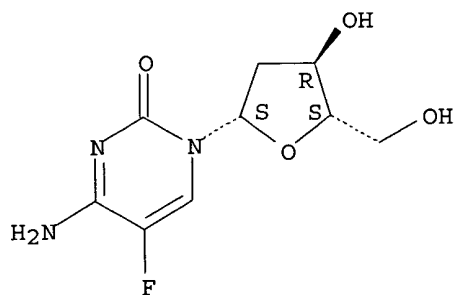
Absolute stereochemistry. Rotation (-).



RN 374107-79-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy-β-L-erythro-pentofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

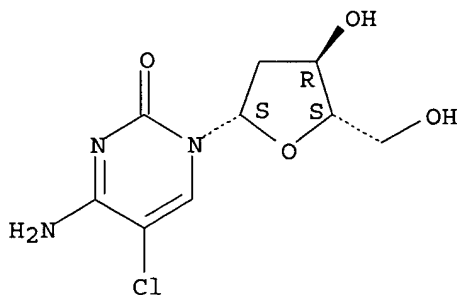
Absolute stereochemistry. Rotation (-).



RN 381719-94-4 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-chloro-1-(2-deoxy-β-L-erythro-pentofuranosyl)- (9CI) (CA INDEX NAME)

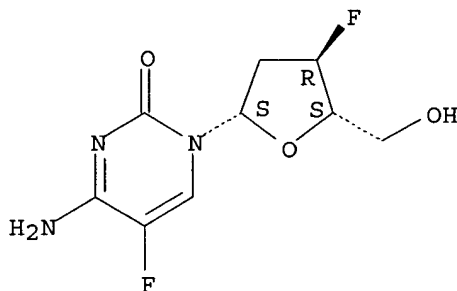
Absolute stereochemistry.



RN 381719-95-5 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2,3-dideoxy-3-fluoro- β -L-erythro-pentofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 11 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:120958 HCAPLUS

DOCUMENT NUMBER: 140:157421

TITLE: 2',3'-dideoxynucleoside analogs for the treatment or prevention of flaviviridae infections

INVENTOR(S): Shi, Junxing; Schinazi, Raymond F.; Striker, Robert

PATENT ASSIGNEE(S): Pharmasset Ltd., Barbados; Emory University; Board of Trustees of the Leland Stanford Junior University

SOURCE: PCT Int. Appl., 86 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004013298	A2	20040212	WO 2003-US24288	20030801
WO 2004013298	A3	20040401		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
 PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
 TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003263978 A1 20040223 AU 2003-263978 20030801
 US 2004067877 A1 20040408 US 2003-632875 20030801
 PRIORITY APPLN. INFO.: US 2002-453715P P 20020801
 US 2002-453716P P 20020801
 WO 2003-US24288 W 20030801

OTHER SOURCE(S): MARPAT 140:157421

AB A method for the treatment or prevention of flaviviridae infections, in particular, **hepatitis C virus** infection, in a host, and in particular, a human, is provided that includes administering an effective amount of a 2',3'-dideoxynucleoside or a pharmaceutically acceptable salt or prodrug thereof, optionally in a pharmaceutically acceptable diluent or excipient. Preparation of compds. of the invention is included.

IC ICM C12N
 CC 1-5 (Pharmacology)
 Section cross-reference(s): 33
 ST dideoxynucleoside deriv prepn **antiviral** flaviviridae;
hepatitis C virus antiviral
 dideoxynucleoside deriv
 IT **Antiviral** agents
 Drug delivery systems
 Flaviviridae
Hepatitis B virus
Hepatitis C virus
 Human
 Human immunodeficiency virus
 (dideoxynucleoside analog preparation for treatment or prevention of flaviviridae infections)
 IT Infection
 (viral; dideoxynucleoside analog preparation for treatment or prevention of flaviviridae infections)
 IT 121154-51-6P **147058-39-7P**
 RL: **PAC (Pharmacological activity)**; RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (dideoxynucleoside analog preparation for treatment or prevention of flaviviridae infections)
 IT **107036-57-7** 121154-51-6D, derivs. **147058-39-7D**, derivs. **160963-15-5** **160963-16-6** **161170-31-6**
 RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
 (dideoxynucleoside analog preparation for treatment or prevention of flaviviridae infections)
 IT 56-92-8, Ceplene 768-94-5, Amantadine 36791-04-5, Ribavirin 62304-98-7, Zadaxin 118390-30-0, Infergen 119567-79-2, Viramidine 198153-51-4, Pegasys 198821-22-6, VX 497 206269-27-4, Levovirin 220581-49-7, Rebif 223603-41-6, ISIS 14803 254750-02-2, IDN-6556 402957-28-2, LY 570310 472960-22-8, Albuferon 632385-00-3, Heptazyme 656836-15-6, IP 501 656836-16-7, XTL 002 656836-17-8, **HCV/MF** 59 656836-18-9, Civacir 656836-19-0, JTK 003
 RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(dideoxynucleoside analog preparation for treatment or prevention of flaviviridae infections, and use with other agents)

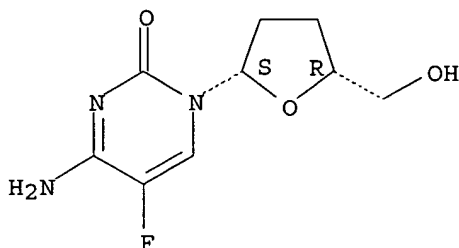
IT 147058-39-7P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (dideoxynucleoside analog preparation for treatment or prevention of flaviviridae infections)

RN 147058-39-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



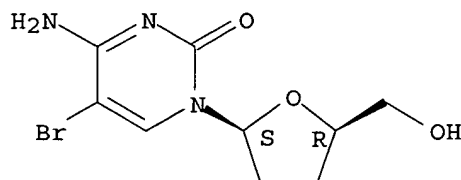
IT 107036-57-7 147058-39-7D, derivs. 160963-15-5
160963-16-6 161170-31-6

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (dideoxynucleoside analog preparation for treatment or prevention of flaviviridae infections)

RN 107036-57-7 HCAPLUS

CN Cytidine, 5-bromo-2',3'-dideoxy- (9CI) (CA INDEX NAME)

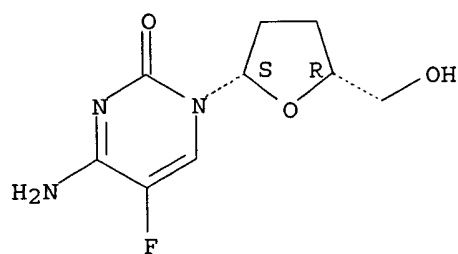
Absolute stereochemistry.



RN 147058-39-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

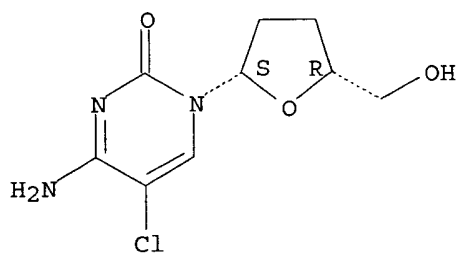
Absolute stereochemistry. Rotation (-).



RN 160963-15-5 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-chloro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

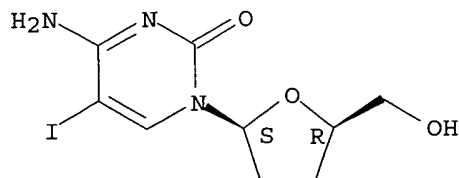
Absolute stereochemistry. Rotation (-).



RN 160963-16-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-iodo-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

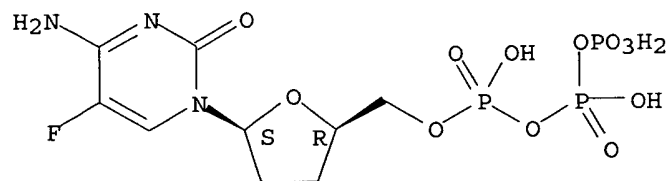
Absolute stereochemistry.



RN 161170-31-6 HCAPLUS

CN Triphosphoric acid, P-[(2R,5S)-[5-(4-amino-5-fluoro-2-oxo-1(2H)-pyrimidinyl)tetrahydro-2-furanyl]methyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L34 ANSWER 12 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:41226 HCAPLUS
 DOCUMENT NUMBER: 140:105321
 TITLE: Methods and compositions relating to isoleucine boroproline compounds
 INVENTOR(S): Adams, Sharlene; Miller, Glenn T.; Jesson, Michael I.; Jones, Barry
 PATENT ASSIGNEE(S): Point Therapeutics, Inc., USA
 SOURCE: PCT Int. Appl., 152 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004658	A2	20040115	WO 2003-US21405	20030709
WO 2004004658	A3	20050804		
W:				
AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZW				
RW:				
GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2491466	AA	20040115	CA 2003-2491466	20030709
AU 2003265264	A1	20040123	AU 2003-265264	20030709
US 2004077601	A1	20040422	US 2003-616694	20030709
US 2005084490	A1	20050421	US 2003-616409	20030709
EP 1578434	A2	20050928	EP 2003-763380	20030709
R:				
AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006507352	T2	20060302	JP 2004-562634	20030709
CN 1802090	A	20060712	CN 2003-821282	20030709
PRIORITY APPLN. INFO.:			US 2002-394856P	P 20020709
			US 2002-414978P	P 20021001
			US 2003-466435P	P 20030428
			WO 2003-US21405	W 20030709

OTHER SOURCE(S): MARPAT 140:105321

AB A method for treating subjects with, inter alia, abnormal cell proliferation or infectious disease using agents of formula (I, AmNHCH(CH(CH3)CH2CH3)COA1R) (where Am and A1 are amino acids and R = organo boronates, organo phosphonates, fluoroalkyl ketones, alphaketos, N-peptioly-O-(acylhydroxylamines), azapeptides, azetidines, fluoroolefins dipeptide isosteres, peptidyl (α -aminoalkyl) phosphonate esters, aminoacyl pyrrolidine-2-nitriles and 4-cyanothiazolidides) is claimed. Methods for stimulating an immune response using the compds. of the invention are also claimed. Compns. containing Ile-boroPro compds. are also provided as are kits containing the compns. The invention embraces the use of these compds. alone or in combination with other therapeutic agents.

IC ICM A61K

CC 1-12 (Pharmacology)

Section cross-reference(s): 15

IT **Hepatitis**

(A; therapeutic methods and compns. relating to isoleucine boroproline

compds. alone or in combination with other drugs, antibodies, or antigens)

IT **Hepatitis**

(B; therapeutic methods and compns. relating to isoleucine boroproline compds. alone or in combination with other drugs, antibodies, or antigens)

IT **Hepatitis**

(C; therapeutic methods and compns. relating to isoleucine boroproline compds. alone or in combination with other drugs, antibodies, or antigens)

IT Infection

(**hepatitis A**; therapeutic methods and compns. relating to isoleucine boroproline compds. alone or in combination with other drugs, antibodies, or antigens)

IT Vaccines

(**hepatitis B**, method of shortening vaccination course; therapeutic methods and compns. relating to isoleucine boroproline compds. alone or in combination with other drugs, antibodies, or antigens)

IT Antibodies and Immunoglobulins

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**hepatitis B**-specific Ig; therapeutic methods and compns. relating to isoleucine boroproline compds. alone or in combination with other drugs, antibodies, or antigens)

IT Infection

(**hepatitis B**; therapeutic methods and compns. relating to isoleucine boroproline compds. alone or in combination with other drugs, antibodies, or antigens)

IT Infection

(**hepatitis C**; therapeutic methods and compns. relating to isoleucine boroproline compds. alone or in combination with other drugs, antibodies, or antigens)

IT Vaccines

(**hepatitis**, method of shortening vaccination course; therapeutic methods and compns. relating to isoleucine boroproline compds. alone or in combination with other drugs, antibodies, or antigens)

IT Acute lymphocytic leukemia

Acute myeloid leukemia

Angiogenesis inhibitors

Anti-infective agents

Antibacterial agents

Antibacterial agents

Antibiotics

Antiemetics

Antimicrobial agents

Antitumor agents

Antiviral agents

Biliary tract, neoplasm

Bladder, neoplasm

Bone, neoplasm

Brain, neoplasm

Central nervous system, neoplasm

Chronic lymphocytic leukemia

Chronic myeloid leukemia

Digestive tract, neoplasm

Drug delivery systems

Esophagus, neoplasm

Eye, neoplasm
 Fungicides
 Head and Neck
 Head and Neck, neoplasm
 Hodgkin's disease
 Human
 Immunodeficiency
 Immunostimulants
 Infection
 Influenza A virus
 Kidney, neoplasm
 Larynx, neoplasm
 Leprosy
 Leukemia
 Liver, neoplasm
 Lymphoma
 Malaria
 Mammary gland, neoplasm
 Melanoma
 Mouth, neoplasm
 Multiple myeloma
 Multiple sclerosis
 Mycosis
 Nausea
 Neoplasm
 Ovary, neoplasm
 Pancreas, neoplasm
 Parasitocides
 Prostate gland, neoplasm
 Radiotherapy
 Respiratory system, neoplasm
 Sarcoma
 Skin, neoplasm
 Staphylococcus
 Stomach, neoplasm
 Testis, neoplasm
 Thyroid gland, neoplasm
 Tuberculosis
 Tuberculostatics
 Urinary system, neoplasm
 Uterus, neoplasm
 Vaccines

(therapeutic methods and compns. relating to isoleucine boroprolone
 compds. alone or in combination with other drugs, antibodies, or
 antigens)

- IT Infection
 (viral; therapeutic methods and compns. relating to
 isoleucine boroprolone compds. alone or in combination with other
 drugs, antibodies, or antigens)
- IT 63527-52-6, Cefotaxime 63585-09-1, Foscarnet sodium 64211-46-7,
 Oxiconazole nitrate 64221-86-9, Imipenem 64221-86-9D, Imipenem,
 derivs. 64485-93-4, Cefotaxime sodium 64544-07-6, Cefuroxime axetil
 64872-77-1, Butoconazole nitrate 64952-97-2, Moxalactam 65025-62-9,
 (-)-Soulattrolide 65052-63-3, Cefetamet 65271-80-9, Mitoxantrone
 65277-42-1, Ketoconazole 65473-14-5, Naftifine hydrochloride
 65899-73-2, Tioconazole 66148-78-5, Temocillin 66309-69-1, Cefotiam
 hydrochloride 66887-96-5, Propikacin 67337-44-4, Sarmoxicillin
 67915-31-5, Terconazole 68401-82-1, Ceftizoxime sodium 68693-30-1,
 Somantadine hydrochloride 68902-57-8, Metioprim 69123-90-6,

Fiacitabine 69123-98-4, Fialuridine 69198-10-3, Metronidazole hydrochloride 69402-03-5, Piridicillin sodium 69521-94-4, Thymosin α -1 69655-05-6, Didanosine 69657-51-8, Acyclovir sodium 69712-56-7, Cefotetan 69756-53-2, Halofantrine 70052-12-9, Eflornithine 70288-86-7, Ivermectin 70458-92-3, Pefloxacin 70458-95-6, Pefloxacin mesylate 70458-96-7, Norfloxacin 70797-11-4, Cefpiramide 71002-10-3, Vidarabine sodium phosphate 71420-79-6, 72275-67-3, Astromicin sulfate 72301-78-1, Zinviroxime 72301-79-2, Enviroxime 72558-82-8, Ceftazidime 72559-06-9, Rifabutin 73334-05-1, Metronidazole phosphate 73384-59-5, Ceftriaxone 73514-87-1, Fosarilate 73816-42-9, Meclocycline sulfosalicylate 74011-58-8, Enoxacin 74356-00-6, Cefotetan disodium 74578-69-1, Ceftriaxone sodium 74682-62-5, Ticarcillin monosodium 74849-93-7, Cefpiramide sodium 75738-58-8, Cefmenoxime hydrochloride 76168-82-6, Ramoplanin 76470-66-1, Loracarbef 76497-13-7, Sultamicillin 76610-84-9, Cefbuperazone 77146-42-0, Chlorhexidine phosphanilate 77181-69-2, Sorivudine 78040-85-4, Coumerymycin 78110-38-0, Aztreonam 78186-33-1, Fumoxicillin 78613-35-1, Amorolfine 78822-40-9, Pirlimycin hydrochloride 78964-85-9, Fosfomycin tromethamine 79350-37-1, Cefixime 79404-91-4, Cilofungin 79660-72-3, Fleroxacin 80168-44-1, Zinoconazole hydrochloride 80214-83-1, Roxithromycin 80621-81-4, Rifaximin 80883-55-2, Enviradene 81103-11-9, Clarithromycin 82410-32-0, Ganciclovir 82419-36-1, Ofloxacin 83038-87-3, Doxycycline fosfatex 83200-96-8D, Carbapenem, derivs. 83905-01-5, Azithromycin 84408-37-7, Desciclovir 84625-61-6, Itraconazole 84880-03-5, Cefpimizole 85287-61-2, Cefpimizole sodium 85721-33-1, Ciprofloxacin 86386-73-4, Fluconazole 86393-37-5, Amifloxacin 86832-68-0, Carumonam sodium 87239-81-4, Cefpodoxime proxetil 87495-31-6, Disoxaril 87806-31-3, Porfimer sodium 88036-80-0, Amifloxacin mesylate 88040-23-7, Cefepime 90849-08-4, Oximonam sodium 90850-05-8, Gloximonomam 90898-90-1, Oximonam 91161-71-6, Terbinafine 91618-36-9, Ibafoxacin 91832-40-5, Cefdinir 92562-88-4 92665-29-7, Cefprozil 93107-08-5, Ciprofloxacin hydrochloride 94088-85-4, Doxycycline calcium 94168-98-6, Rifametan 95058-81-4, Gemcitabine 96036-03-2, Meropenem 96128-89-1, Erythromycin acistrate 97519-39-6, Ceftibuten 97673-66-0, Trospectomycin sulfate 97682-44-5, Irinotecan 98079-51-7, Lomefloxacin 98079-52-8, Lomefloxacin hydrochloride 98753-19-6, Cefpirome sulfate 100234-70-6, Resorcinomycin A 100490-36-6, Tosufloxacin 100680-33-9, Cefuroxime pivoxetil 101828-21-1, Butenafine 102426-96-0, Paldimycin 103060-53-3, Daptomycin 104227-87-4, Famciclovir 104456-95-3, Ciconazole 105784-61-0, Temafloxacin hydrochloride 105956-99-8, Clinafloxacin hydrochloride 106941-25-7, Adefovir 107648-80-6, Cefepime hydrochloride 107910-75-8, Ganciclovir sodium 108319-06-8, Temafloxacin 110042-95-0, Acemannan 110588-57-3, Saperconazole 110871-86-8, Sparfloxacin 110942-02-4, Aldesleukin 112362-50-2, Dalfoprstin 113102-19-5, Rifamexil 113852-37-2, Cidofovir 114394-67-1, Lomefloxacin mesylate 114977-28-5, Taxotere 117091-64-2, Etoposide phosphate 117211-03-7, Cefetecol 119413-54-6, Topotecan hydrochloride 120138-50-3, Quinupristin 120410-24-4, Biapenem 120788-07-0, Sulopenem 122111-03-9, Gemcitabine hydrochloride 124436-59-5, Pirodavis 124832-27-5, Valacyclovir hydrochloride 125317-39-7, Vinorelbine tartrate 127464-60-2, Vascular endothelial growth factor 127759-89-1, Lobucavir 127779-20-8, Saquinavir 127785-64-2, Basifungin 129618-40-2, Nevirapine 130167-69-0, Pegaspargase 132210-43-6, Cipamfylline 134678-17-4, Lamivudine 136817-59-9, Delavirdine 137487-62-8, Alvircept sudotox 138540-32-6, Atevirdine mesylate 139442-47-0, LFM-A 12 141611-76-9, Sanfetrinem sodium 142217-69-4, Entecavir 142340-99-6, Adefovir dipivoxil 142632-32-4, (+)Calanolide A 143491-57-0, Emtricitabine 147221-93-0,

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156586-89-9, Panorex 159989-64-7, Nelfinavir 163252-36-6, Clevudine
163661-45-8, (-)-Calanolide A 164301-51-3, CNI-1493 167869-21-8,
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213327-37-8, Oregovomab 216503-57-0, Campath 216503-58-1, Mitumomab
216974-75-3, Avastin 220578-59-6, Mylotarg 339150-51-5, CeaVac
339150-82-2, LymphoCide 339151-95-0, MDX-22 339151-96-1, MDX-447
339152-71-5, MDX-210 339286-23-6, Gliomab-H 339286-24-7, GNI-250
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645416-54-2, AG 1458 645417-10-3, UK 292 645417-21-6, BAY 38-9502
646031-42-7, Celogovab 646032-07-7, ZamyI

RL: **PAC (Pharmacological activity); THU (Therapeutic use);** BIOL (Biological study); USES (Uses)

(therapeutic methods and compns. relating to isoleucine boroproline
compds. alone or in combination with other drugs, antibodies, or
antigens)

IT 69123-90-6, Fiacitabine

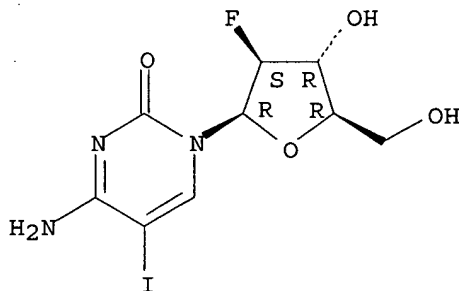
RL: **PAC (Pharmacological activity); THU (Therapeutic use);** BIOL (Biological study); USES (Uses)

(therapeutic methods and compns. relating to isoleucine boroproline
compds. alone or in combination with other drugs, antibodies, or
antigens)

RN 69123-90-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy-2-fluoro- β -D-arabinofuranosyl)-
5-iodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L34 ANSWER 13 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:714301 HCAPLUS

DOCUMENT NUMBER: 140:199600

TITLE: Synthesis and **Antiviral** Evaluation of
2',3'-Dideoxy-2'-fluoro-3'-C-hydroxymethyl- β -D-
arabinofuranosyl Pyrimidine Nucleosides

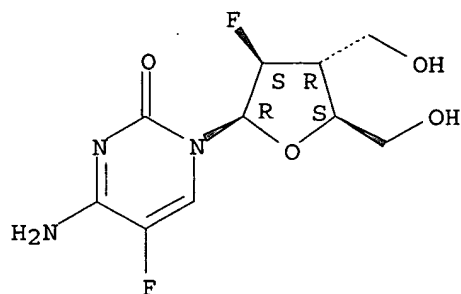
AUTHOR(S): Hassan, Abdalla E. A.; Pai, Balakrina S.; Lostia,
Stefania; Stuyver, Lieven; Otto, Michael J.; Schinazi,
Raymond F.; Watanabe, Kyoichi A.

CORPORATE SOURCE: Pharmasset Inc., Tucker, GA, 30084, USA

SOURCE: Nucleosides, Nucleotides & Nucleic Acids (2003),

22(5-8), 891-894
CODEN: NNNAFY; ISSN: 1525-7770
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:199600
AB The synthesis and anti-HBV and anti-HIV activity of a number of
2',3'-dideoxy-2'-fluoro-3'-C-hydroxymethyl- β -D-arabinofuranosyl
pyrimidine nucleosides are reported.
CC 33-9 (Carbohydrates)
Section cross-reference(s): 1
ST fluoro hydroxymethylarabinofuranosyl pyrimidine nucleoside prepn HIV HBV
antiviral
IT Anti-AIDS agents
Antiviral agents
Fluorination
Hepatitis B virus
Human
Human immunodeficiency virus
(synthesis and **antiviral** evaluation of dideoxy-2'-fluoro-3'-
hydroxymethyl- β -D-arabinofuranosyl pyrimidine nucleosides)
IT Pyrimidine nucleosides
RL: PAC (Pharmacological activity); BIOL (Biological study)
(synthesis and **antiviral** evaluation of dideoxy-2'-fluoro-3'-
hydroxymethyl- β -D-arabinofuranosyl pyrimidine nucleosides)
IT 181045-04-5 181045-09-0 **367491-98-3**
RL: **PAC (Pharmacological activity)**; BIOL (Biological study)
(synthesis and **antiviral** evaluation of dideoxy-2'-fluoro-3'-
hydroxymethyl- β -D-arabinofuranosyl pyrimidine nucleosides)
IT 7288-28-0 41108-04-7 56653-26-0 146035-67-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and **antiviral** evaluation of dideoxy-2'-fluoro-3'-
hydroxymethyl- β -D-arabinofuranosyl pyrimidine nucleosides)
IT 69827-89-0P 69827-90-3P 663170-37-4P 663170-38-5P 663170-39-6P
663170-40-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(synthesis and **antiviral** evaluation of dideoxy-2'-fluoro-3'-
hydroxymethyl- β -D-arabinofuranosyl pyrimidine nucleosides)
IT **367491-98-3**
RL: **PAC (Pharmacological activity)**; BIOL (Biological study)
(synthesis and **antiviral** evaluation of dideoxy-2'-fluoro-3'-
hydroxymethyl- β -D-arabinofuranosyl pyrimidine nucleosides)
RN 367491-98-3 HCAPLUS
CN 2(1H)-Pyrimidinone, 4-amino-1-[2,3-dideoxy-2-fluoro-3-(hydroxymethyl)-
 β -D-arabinofuranosyl]-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 14 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:656522 HCAPLUS

DOCUMENT NUMBER: 139:173779

TITLE: Modified fluorinated nucleoside analogs as **antiviral agents**

INVENTOR(S): Stuyver, Lieven J.; Shi, Jinxing; Watanabe, Kyoichi A.

PATENT ASSIGNEE(S): Pharmasset Ltd., Barbados

SOURCE: PCT Int. Appl., 234 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068162	A2	20030821	WO 2003-US4379	20030213
WO 2003068162	A3	20040311		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2476279	AA	20030821	CA 2003-2476279	20030213
AU 2003217402	A1	20030904	AU 2003-217402	20030213
US 2004002476	A1	20040101	US 2003-366144	20030213
EP 1480982	A2	20041201	EP 2003-713447	20030213
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007712	A	20050524	BR 2003-7712	20030213
CN 1646534	A	20050727	CN 2003-808372	20030213
JP 2005522443	T2	20050728	JP 2003-567347	20030213
US 2003225029	A1	20031204	US 2003-367388	20030214
CN 1646129	A	20050727	CN 2003-808385	20030214
ZA 2004006858	A	20050701	ZA 2004-6858	20040827
PRIORITY APPLN. INFO.:			US 2002-357411P	P 20020214
			US 2002-358140P	P 20020220
			WO 2003-US4379	W 20030213

OTHER SOURCE(S): MARPAT 139:173779

- AB The invention is a compound, composition, use for and a method of treating Flaviviridae (Hepacivirus, Flavivirus, Pestivirus) infections, including BVDV and HCV, or abnormal cellular proliferation, including malignant tumors, in a host including animals, and especially humans, using a ss-D or ss-L nucleoside or their pharmaceutically acceptable salt or prodrug thereof.
- IC ICM A61K
- CC 1-5 (Pharmacology)
Section cross-reference(s): 63
- ST **antiviral** fluorinated nucleoside analog gemcitabine flaviviridae infection
- IT Drug delivery systems
(capsules; fluorinated nucleoside analogs as **antiviral** agents)
- IT Antitumor agents
Antiviral agents
Cell proliferation
Drug delivery systems
Flavivirus
Hepatitis C virus
Hepatitis C-like viruses
Human
Neoplasm
Pestivirus
(fluorinated nucleoside analogs as **antiviral** agents)
- IT Nucleosides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fluorinated nucleoside analogs as **antiviral** agents)
- IT Drug delivery systems
(prodrugs; fluorinated nucleoside analogs as **antiviral** agents)
- IT Drug delivery systems
(tablets; fluorinated nucleoside analogs as **antiviral** agents)
- IT Drug delivery systems
(unit doses; fluorinated nucleoside analogs as **antiviral** agents)
- IT Infection
(**viral**; fluorinated nucleoside analogs as **antiviral** agents)
- IT 122799-38-6P **581772-30-7P**
RL: **PAC (Pharmacological activity)**; RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(fluorinated nucleoside analogs as **antiviral** agents)
- IT 784-71-4, 2'-Deoxy-2'-fluorouridine 10212-20-1, 2'-Deoxy-2'-FluoroCytidine
RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(fluorinated nucleoside analogs as **antiviral** agents)
- IT **80791-93-1P** 95058-81-4P, Gemcitabine **97716-26-2P**
182495-80-3P **581772-31-8P** 581772-34-1P
RL: **PAC (Pharmacological activity)**; SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(fluorinated nucleoside analogs as **antiviral** agents)
- IT 171233-40-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(fluorinated nucleoside analogs as **antiviral** agents)

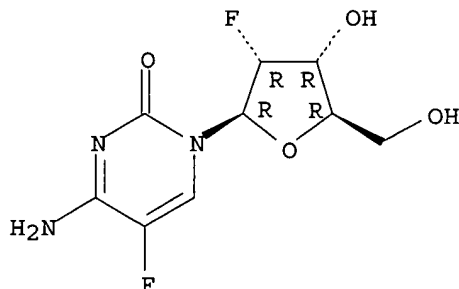
IT 581772-30-7P

RL: **PAC (Pharmacological activity)**; RCT (Reactant); SPN
(Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological
study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(fluorinated nucleoside analogs as **antiviral** agents)

RN 581772-30-7 HCAPLUS

CN Cytidine, 2'-deoxy-2',5-difluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



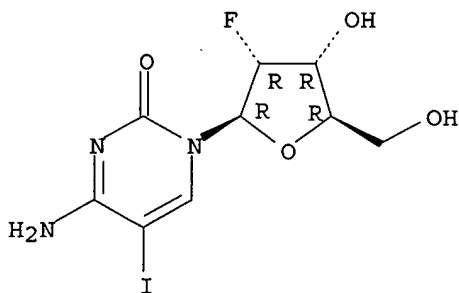
IT 80791-93-1P 97716-26-2P 581772-31-8P

RL: **PAC (Pharmacological activity)**; SPN (Synthetic preparation);
THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)
(fluorinated nucleoside analogs as **antiviral** agents)

RN 80791-93-1 HCAPLUS

CN Cytidine, 2'-deoxy-2'-fluoro-5-iodo- (9CI) (CA INDEX NAME)

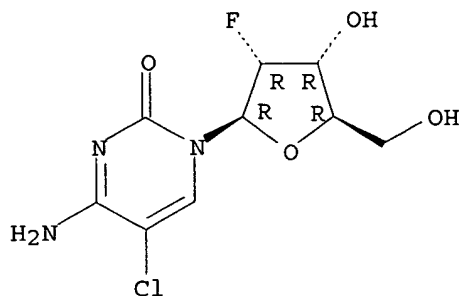
Absolute stereochemistry.



RN 97716-26-2 HCAPLUS

CN Cytidine, 5-chloro-2'-deoxy-2'-fluoro- (9CI) (CA INDEX NAME)

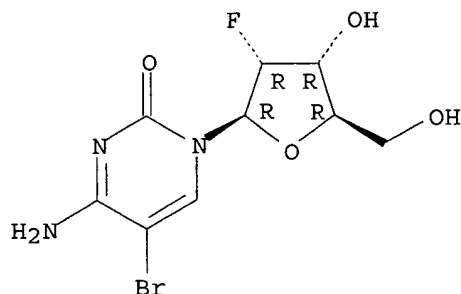
Absolute stereochemistry.



RN 581772-31-8 HCAPLUS

CN Cytidine, 5-bromo-2'-deoxy-2'-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L34 ANSWER 15 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:492694 HCAPLUS

DOCUMENT NUMBER: 139:47125

TITLE: Induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and drug screening method

INVENTOR(S): Loeb, Lawrence A.; Mullins, James I.

PATENT ASSIGNEE(S): University of Washington, USA

SOURCE: U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of U.S. Ser. No. 958,065.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003119764	A1	20030626	US 2000-522373	20000310
US 6887707	B2	20050503		
US 6063628	A	20000516	US 1997-958065	19971027
US 2005187180	A1	20050825	US 2005-98796	20050404
PRIORITY APPLN. INFO.:			US 1996-29404P	P 19961028
			US 1997-40535P	P 19970227
			US 1997-958065	A2 19971027
			US 2000-522373	A3 20000310

AB The present invention is directed to the identification and use of

ribonucleoside analogs to induce the mutation of an RNA virus, including BVDV, HIV and HCV, or a virus which otherwise replicates through an RNA intermediate. The increase in the mutation rate of the virus results in reduced viability of progeny generations of the virus, thereby inhibiting viral replication. In addition to these methods and related comps., the invention provides methods and combinatorial chemical libraries for screening ribonucleoside analogs for mutagenic potential.

- IC ICM A61K048-00
- ICS A61K031-7072; A61K031-7076; C12N007-00; C12N015-86
- INCL 514044000; 514045000; 514049000; 435456000; 435235100
- CC 1-5 (Pharmacology)
- Section cross-reference(s): 63
- ST ribonucleoside analog virus mutation **antiviral**; screening **antiviral** ribonucleoside analog virus mutation; combinatorial library **antiviral** ribonucleoside analog
- IT **Hepatitis**
(B; induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and drug screening method)
- IT **Hepatitis**
(C; induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and drug screening method)
- IT Antitumor agents
(T-cell leukemia; induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and drug screening method)
- IT mRNA
RL: BSU (Biological study, unclassified); BIOL (Biological study) (analogs; induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and drug screening method)
- IT Mass spectrometry
NMR (nuclear magnetic resonance)
(determining structure of ribonucleoside analog monomers by; induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and drug screening method)
- IT Nucleosides, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study) (enantio-specific analog; induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and drug screening method)
- IT Infection
(**hepatitis** B; induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and drug screening method)
- IT Infection
(**hepatitis** C; induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and drug screening method)
- IT Animal tissue culture
Anti-AIDS agents
Antiviral agents
Bovine diarrhea virus
Combinatorial library
Coronavirus
Dengue virus
Drug delivery systems
Drug screening

Feline immunodeficiency virus

Feline leukemia virus

Hepatitis A virus

Hepatitis B virus

Hepatitis C virus

Human

Human T-lymphotropic virus 1

Human T-lymphotropic virus 2

Human immunodeficiency virus

Human immunodeficiency virus 1

Human immunodeficiency virus 2

Influenza virus

RNA viruses

Respiratory syncytial virus

Retroviridae

Simian immunodeficiency virus

Vesicular stomatitis virus

(induction of **viral** mutation by incorporation of miscoding
ribonucleoside analogs into **viral** RNA, and drug screening
method)

IT DNA

RNA

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(induction of **viral** mutation by incorporation of miscoding
ribonucleoside analogs into **viral** RNA, and drug screening
method)

IT Nucleoside analogs

RL: BSU (Biological study, unclassified); CUS (Combinatorial use); THU
(Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study);
USES (Uses)

(induction of **viral** mutation by incorporation of miscoding
ribonucleoside analogs into **viral** RNA, and drug screening
method)

IT Mutagenesis

(method of inducing; induction of **viral** mutation by
incorporation of miscoding ribonucleoside analogs into **viral**
RNA, and drug screening method)

IT Mutagens

(mutagenic potential; induction of **viral** mutation by
incorporation of miscoding ribonucleoside analogs into **viral**
RNA, and drug screening method)

IT Virus

(mutation rate; induction of **viral** mutation by incorporation
of miscoding ribonucleoside analogs into **viral** RNA, and drug
screening method)

IT Hydrolysis

(of ribonucleotide polymer, to yield ribonucleoside analog monomers;
induction of **viral** mutation by incorporation of miscoding
ribonucleoside analogs into **viral** RNA, and drug screening
method)

IT Drug delivery systems

(oral; induction of **viral** mutation by incorporation of
miscoding ribonucleoside analogs into **viral** RNA, and drug
screening method)

IT Drug delivery systems

(parenterals; induction of **viral** mutation by incorporation of
miscoding ribonucleoside analogs into **viral** RNA, and drug
screening method)

IT Reactive oxygen species

- RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and drug screening method)
- IT RNA formation
(replication, **viral**, inhibiting; induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and drug screening method)
- IT Nucleic acids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(templates; induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and drug screening method)
- IT Animals
(therapy of; induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and drug screening method)
- IT 65-46-3, Cytidine 66-22-8, Uracil, biological studies 73-24-5, Adenine, biological studies 73-40-5, Guanine
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(RNA nucleoside analog replacement of; induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and drug screening method)
- IT 9014-24-8, RNA polymerase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(and RNA polymerase II; induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and drug screening method)
- IT 65-71-4, Thymine 71-30-7, Cytosine 7732-18-5, Water, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and drug screening method)
- IT 58-61-7D, Adenosine, derivs. 58-96-8D, Uridine, derivs. 65-46-3D, Cytidine, derivs. 118-00-3D, Guanosine, derivs. 957-77-7, 5-Hydroxyuridine 957-77-7D, 5-Hydroxyuridine, derivs. 1867-73-8 1867-73-8D, derivs. 2140-64-9, 3-Methylcytidine 2140-64-9D, 3-Methylcytidine, derivs. 2140-69-4, 3-Methyluridine 2140-69-4D, 3-Methyluridine, derivs. 2149-76-0, 5-Aminouridine 2149-76-0D, 5-Aminouridine, derivs. **3066-86-2**, 5-Bromocytidine **3066-86-2D**, 5-Bromocytidine, derivs. 3868-31-3, 8-Hydroxyguanosine 3868-31-3D, 8-Hydroxyguanosine, derivs. 3868-32-4, 8-Aminoguanosine 3868-32-4D, 8-Aminoguanosine, derivs. 7803-88-5 7803-88-5D, derivs. 13007-43-7 13007-43-7D, derivs. 23899-77-6, 5-Aminocytidine 23899-77-6D, 5-Aminocytidine, derivs. **25130-29-4**, 5-Chlorocytidine **25130-29-4D**, 5-Chlorocytidine, derivs. 33962-59-3 33962-59-3D, derivs. 34218-77-4 34218-77-4D, derivs. 39007-51-7 39007-51-7D, derivs. 39007-52-8 39007-52-8D, derivs. 39638-73-8 39638-73-8D, derivs. 39708-01-5 39708-01-5D, derivs. 53337-88-5 53337-88-5D, derivs. 53337-89-6 53337-89-6D, derivs. 57294-74-3 57294-74-3D, derivs. 59495-20-4 59495-20-4D, derivs. 72055-62-0, 3-Methyladenosine 72055-62-0D, 3-Methyladenosine, derivs. 82773-20-4 82773-20-4D, derivs. 100997-68-0 100997-68-0D, derivs. 108060-85-1 108060-85-1D, derivs. 137248-64-7 137248-64-7D, derivs. 207340-54-3 207340-54-3D, derivs. 207340-56-5 207340-56-5D, derivs. 207340-58-7 207340-58-7D, derivs.
RL: BSU (Biological study, unclassified); CUS (Combinatorial use); **THU (Therapeutic use)**; BIOL (Biological study); CMBI

(Combinatorial study); USES (Uses)

(induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and drug screening method)

IT 7782-44-7D, Oxygen, free radicals

RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction, modification of ribonucleoside analogs by; induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and drug screening method)

IT 3066-86-2, 5-Bromocytidine 3066-86-2D, 5-Bromocytidine, derivs. 25130-29-4, 5-Chlorocytidine 25130-29-4D, 5-Chlorocytidine, derivs.

RL: BSU (Biological study, unclassified); CUS (Combinatorial use);

THU (Therapeutic use); BIOL (Biological study); CMBI

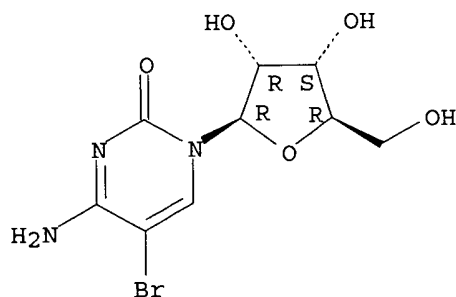
(Combinatorial study); USES (Uses)

(induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and drug screening method)

RN 3066-86-2 HCAPLUS

CN Cytidine, 5-bromo- (7CI, 8CI, 9CI) (CA INDEX NAME)

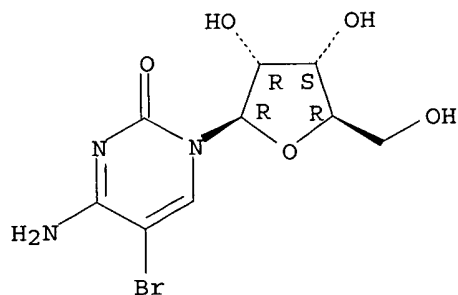
Absolute stereochemistry.



RN 3066-86-2 HCAPLUS

CN Cytidine, 5-bromo- (7CI, 8CI, 9CI) (CA INDEX NAME)

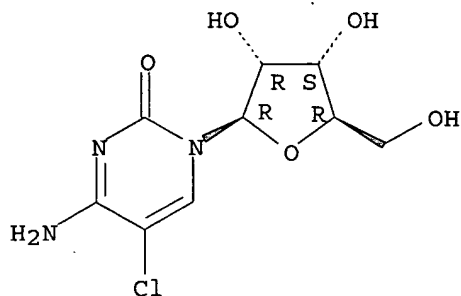
Absolute stereochemistry.



RN 25130-29-4 HCAPLUS

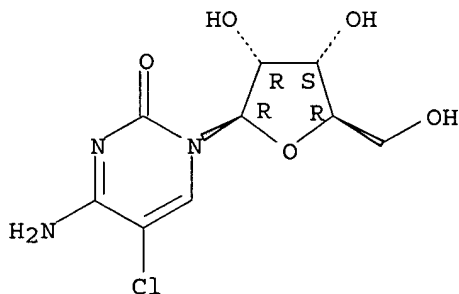
CN Cytidine, 5-chloro- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 25130-29-4 HCAPLUS
CN Cytidine, 5-chloro- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 16 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:133429 HCAPLUS
DOCUMENT NUMBER: 138:210275
TITLE: Immunomodulatory compositions, formulations, and methods for use thereof
INVENTOR(S): Fearon, Karen L.; Dina, Dino
PATENT ASSIGNEE(S): Dynavax Technologies Corporation, USA
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003014316	A2	20030220	WO 2002-US25123	20020807
WO 2003014316	A3	20040311		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,				

KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
CA 2456328 AA 20030220 CA 2002-2456328 20020807
US 2003133988 A1 20030717 US 2002-214799 20020807
EP 1420829 A2 20040526 EP 2002-761284 20020807
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
JP 2005527465 T2 20050915 JP 2003-519446 20020807
PRIORITY APPLN. INFO.: US 2001-310743P P 20010807
US 2001-335263P P 20011025
WO 2002-US25123 W 20020807

OTHER SOURCE(S): MARPAT 138:210275

AB The invention provides new compns. and methods for immunomodulation of individuals. Immunomodulation is accomplished by administration of immunomodulatory polynucleotide/microcarrier (IMO/MC) complexes comprising 3-6mer immunomodulatory oligonucleotides. The IMO/MC complexes may be covalently or non-covalently bound. Also provided are immunomodulatory compns. comprising a 3-6mer IMO encapsulated in an MC.

IC ICM C12N

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 1, 15

IT Allergy

Allergy inhibitors

Antiasthmatics

Asthma

Epitopes

Hepatitis B virus

Hepatitis C virus

Human

Human herpesvirus

Immunomodulators

Immunostimulants

Infection

Malaria

Papillomavirus

Respiratory syncytial virus

Vaccines

(immunomodulatory oligonucleotide compns. for use with microcarriers)

IT Infection

(**viral**; immunomodulatory oligonucleotide compns. for use with microcarriers)

IT 216769-36-7 216769-42-5 216769-47-0 352016-59-2 387819-74-1

482624-41-9 497917-77-8 499212-77-0 499212-78-1 499212-79-2

499212-80-5 499212-81-6 499212-82-7 499212-83-8 499212-84-9

499212-86-1 499212-87-2 499212-88-3 499212-89-4 499212-90-7

499212-91-8 499212-92-9 **499212-93-0** 499212-94-1

499212-95-2 499212-96-3 499212-97-4 499212-98-5 499212-99-6

499213-00-2

RL: **PAC (Pharmacological activity)**; PRP (Properties); **THU**

(**Therapeutic use**); BIOL (Biological study); USES (Uses)

(immunomodulatory oligonucleotide compns. for use with microcarriers)

IT **499212-93-0**

RL: **PAC (Pharmacological activity)**; PRP (Properties); **THU**

(**Therapeutic use**); BIOL (Biological study); USES (Uses)

(immunomodulatory oligonucleotide compns. for use with microcarriers)

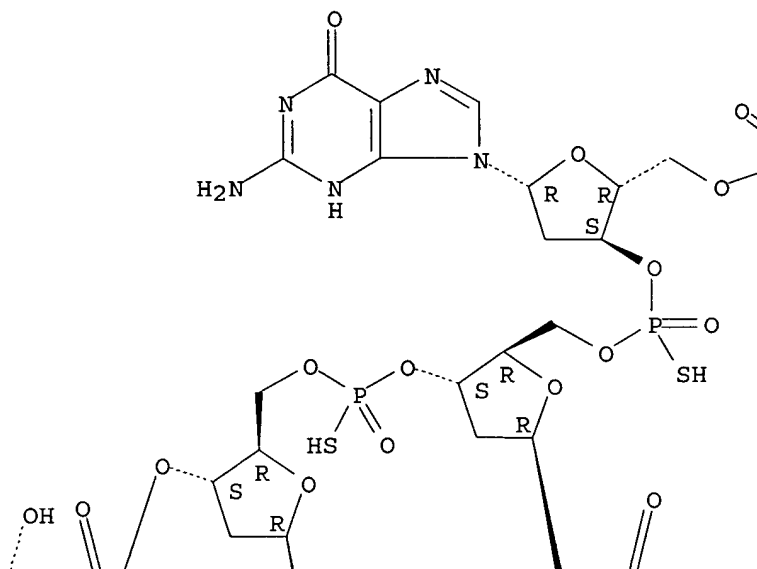
RN 499212-93-0 HCAPLUS

CN Thymidine, P-thiothymidylyl-(3'→5')-5-bromo-2'-deoxy-P-thiocytidylyl-(3'→5')-2'-deoxy-P-thioguanidylyl-(3'→5')-P-

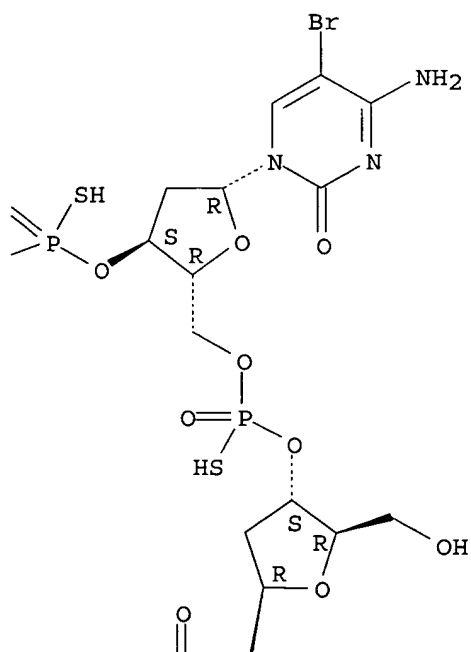
thiothymidyl-(3'→5')-P-thiothymidyl-(3'→5')- (9CI) (CA
INDEX NAME)

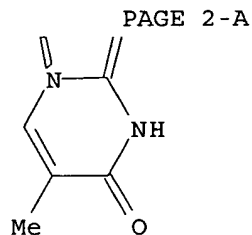
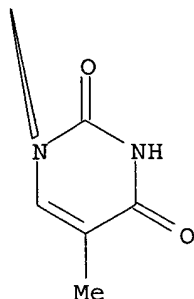
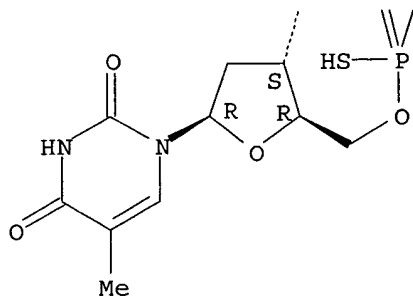
Absolute stereochemistry.

PAGE 1-A

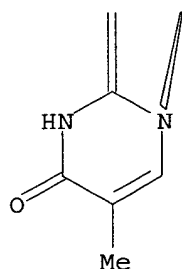


PAGE 1-B





PAGE 2-B



L34 ANSWER 17 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:964200 HCAPLUS

DOCUMENT NUMBER: 138:24920

TITLE: Preparation of 4'-substituted nucleosides as **antiviral** agents

INVENTOR(S): Devos, Rene Robert; Hobbs, Christopher John; Jiang, Wen-Rong; Martin, Joseph Armstrong; Merrett, John Herbert; Najera, Isabel; Shimma, Nobuo; Tsukuda, Takuo

PATENT ASSIGNEE(S): F. Hoffmann-La Roche AG, Switz.

SOURCE: PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

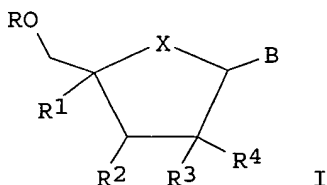
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002100415	A2	20021219	WO 2002-EP6256	20020607
WO 2002100415	A3	20030807		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,

KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,
GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,
GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2449572	AA	20021219	CA 2002-2449572	20020607
NZ 529695	A	20031219	NZ 2002-529695	20020607
EP 1404347	A2	20040407	EP 2002-747356	20020607
EP 1404347	B1	20060118		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002010350	A	20040720	BR 2002-10350	20020607
CN 1516590	A	20040728	CN 2002-811848	20020607
JP 2004536817	T2	20041209	JP 2003-503236	20020607
AT 315938	E	20060215	AT 2002-747356	20020607
ES 2256494	T3	20060716	ES 2002-2747356	20020607
US 2003236216	A1	20031225	US 2002-167106	20020611
US 6784166	B2	20040831		
ZA 2003009169	A	20050225	ZA 2003-9169	20031125
BG 108439	A	20050331	BG 2003-108439	20031212
US 2004266722	A1	20041230	US 2004-891967	20040715
PRIORITY APPLN. INFO.:			GB 2001-14286	A 20010612
			WO 2002-EP6256	W 20020607
			US 2002-167106	A3 20020611
OTHER SOURCE(S):		MARPAT 138:24920		
GI				



AB The present invention relates to the preparation of 4'-substituted nucleosides I, wherein R is hydrogen or -[P(O)(OH)-O]_nH and n is 1-3; R₁ is alkyl, alkenyl, alkynyl, haloalkyl, alkylcarbonyl, alkoxycarbonyl, hydroxyalkyl, alkoxyalkyl, alkoxy, cyano, azido, hydroxyiminomethyl, alkoxyiminomethyl, halogen, alkylcarbonylamino, alkylaminocarbonyl, azidoalkyl, aminomethyl, alkylaminomethyl, dialkylaminomethyl or heterocyclyl; R₂ is hydrogen, hydroxy, amino, alkyl, hydroxyalkyl, alkoxy, halogen, cyano, or azido; R₃ and R₄ are hydrogen, hydroxy, alkoxy, halogen or hydroxyalkyl, provided that at least one of R₃ and R₄ is hydrogen; or R₃ and R₄ together represent =CH₂ or =N-OH, or R₃ and R₄ both represent fluorine; X is O, S or CH₂; B is 9-purinyl or 1-pyrimidyl residues, nucleobase; for the treatment of diseases mediated by the **Hepatitis C virus (HCV)**, for the preparation of a medicament for such treatment and to pharmaceutical compns. containing such compds. Thus, 4'-C-azidocytidine was prepared and tested in vivo in patients as **antiviral** agent. For oral administration, a daily dosage of between about 0.01 and about 100 mg/kg body weight per day should be appropriate in mono-therapy and/or in combination therapy. A preferred daily dosage is between about 0.1 and about 500 mg/kg body weight, more preferred 0.1 and about 100 mg/kg body weight and most preferred 1.0 and about 100 mg/kg body weight per day. A typical preparation will contain from about 5% to about 95% active compound (weight/weight) . The daily dosage can be

administered as a single dosage or in divided dosages, typically between 1 and 5 dosages per day.

IC ICM A61K031-7068

ICS A61K031-7072; A61K031-7076; A61K031-708; C07H019-06; C07H019-16; A61P031-14

CC 33-9 (Carbohydrates)

Section cross-reference(s): 1, 7, 63

ST nucleoside prepn **antiviral** human luciferase cytotoxicity

IT **Antiviral** agents

Drugs

Hepatitis C virus

Human

Therapy

(preparation and cytotoxicity of 4'-substituted nucleosides as **antiviral** agents)

IT Nucleosides, preparation

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation and cytotoxicity of 4'-substituted nucleosides as **antiviral** agents)

IT Infection

(**viral**; preparation and cytotoxicity of 4'-substituted nucleosides as **antiviral** agents)

IT 61869-41-8, Renilla luciferase

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(preparation and cytotoxicity of 4'-substituted nucleosides as **antiviral** agents)

IT 68707-89-1P 130108-72-4P 130108-73-5P 130108-77-9P 139442-01-6P
232589-06-9P 232591-21-8P 478182-29-5P 478182-31-9P 478182-32-0P
478182-33-1P 478182-34-2P **478182-35-3P**

RL: **PAC (Pharmacological activity)**; SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation and cytotoxicity of 4'-substituted nucleosides as **antiviral** agents)

IT 288-88-0, 1H-1,2,4-Triazole 362-43-6 173846-42-9 232588-98-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation and cytotoxicity of 4'-substituted nucleosides as **antiviral** agents)

IT 14259-58-6P 14365-63-0P 14671-65-9P 139419-02-6P 232588-97-5P
232589-01-4P 232589-02-5P 232589-04-7P 478182-26-2P 478182-27-3P
478182-28-4P 478182-30-8P 478182-36-4P 478182-37-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and cytotoxicity of 4'-substituted nucleosides as **antiviral** agents)

IT **478182-35-3P**

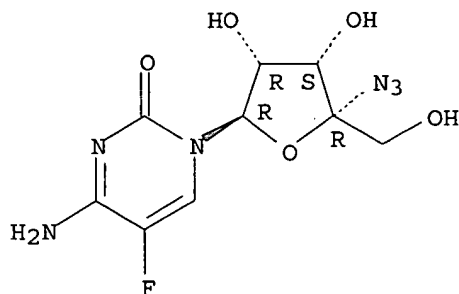
RL: **PAC (Pharmacological activity)**; SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation and cytotoxicity of 4'-substituted nucleosides as **antiviral** agents)

RN 478182-35-3 HCAPLUS

CN Cytidine, 4'-C-azido-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L34 ANSWER 18 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:832613 HCAPLUS

DOCUMENT NUMBER: 137:333119

TITLE: 3-Aminopyridine-2-carboxyaldehyde thiosemicarbazones
and methods using them for treating *viral*
and fungal infectionsINVENTOR(S): King, Ivan C.; Doyle, Terrence W.; Sznol, Mario;
Sartorelli, Alan C.; Cheng, Yung-Chi

PATENT ASSIGNEE(S): Vion Pharmaceuticals, Inc., USA; Yale University

SOURCE: PCT Int. Appl., 68 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085358	A2	20021031	WO 2002-US12358	20020418
WO 2002085358	A3	20021219		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002188011	A1	20021212	US 2002-126050	20020418
US 6911460	B2	20050628		
CN 1503669	A	20040609	CN 2002-808591	20020418
US 2005261251	A1	20051124	US 2005-93648	20050330
PRIORITY APPLN. INFO.:			US 2001-285559P	P 20010420
			US 2002-126050	A3 20020418

OTHER SOURCE(S): MARPAT 137:333119

AB The invention provides methods for treating viral or fungal infections using 3-aminopyridine-2-carboxyaldehyde thiosemicarbazone (3-AP) and 3-amino-4-methylpyridine-2-carboxyaldehyde thiosemicarbazone (3-AMP), and prodrug forms thereof, as well as pharmaceutical compns. comprising these compds. Preparation of compds. of the invention is described.

IC ICM A61K031-44

CC 1-5 (Pharmacology)

Section cross-reference(s): 27, 63

IT Drug interactions

(additive; aminopyridinecarboxyaldehyde thiosemicarbazones for treatment of **viral** and fungal infections)

IT Anti-AIDS agents

Antiviral agents

Aspergillus
Blastomyces dermatitidis
Candida albicans
Coccidioides immitis
Cryptococcus neoformans
Cytomegalovirus
Dengue virus
Drug delivery systems
Epidermophyton
Flavivirus
Fungicides
Hepatitis B virus
Hepatitis C virus
Histoplasma capsulatum
Human
Human T-lymphotropic virus 1
Human T-lymphotropic virus 2
Human adenovirus
Human herpesvirus
Human herpesvirus 1
Human herpesvirus 2
Human herpesvirus 3
Human herpesvirus 4
Human herpesvirus 8
Human immunodeficiency virus
Human immunodeficiency virus 1
Human immunodeficiency virus 2
Human papillomavirus
Immunomodulators
Japanese encephalitis virus
Malassezia furfur
Microsporum
Mycosis
Piedraia hortae
Respiratory syncytial virus
Trichophyton
Trichosporon cutaneum
West Nile virus
Yellow fever virus

(aminopyridinecarboxyaldehyde thiosemicarbazones for treatment of **viral** and fungal infections)

IT CD4 (antigen)

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(aminopyridinecarboxyaldehyde thiosemicarbazones for treatment of **viral** and fungal infections)

IT Acyclonucleosides

Interferons

Interleukin 2

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(aminopyridinecarboxyaldehyde thiosemicarbazones for treatment of **viral** and fungal infections)

IT Lipids, biological studies

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

- (complexes, with amphotericin B; aminopyridinecarboxyaldehyde thiosemicarbazones for treatment of **viral** and fungal infections)
- IT Nucleosides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dideoxy; aminopyridinecarboxyaldehyde thiosemicarbazones for treatment of **viral** and fungal infections)
- IT Drug delivery systems
(liposomes, liposomal amphotericin B; aminopyridinecarboxyaldehyde thiosemicarbazones for treatment of **viral** and fungal infections)
- IT Biological transport
(nucleoside transport inhibitors; aminopyridinecarboxyaldehyde thiosemicarbazones for treatment of **viral** and fungal infections)
- IT Drug delivery systems
(prodrugs; aminopyridinecarboxyaldehyde thiosemicarbazones for treatment of **viral** and fungal infections)
- IT Drug interactions
(synergistic; aminopyridinecarboxyaldehyde thiosemicarbazones for treatment of **viral** and fungal infections)
- IT Nucleosides, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(transport inhibitors; aminopyridinecarboxyaldehyde thiosemicarbazones for treatment of **viral** and fungal infections)
- IT Infection
(**viral**; aminopyridinecarboxyaldehyde thiosemicarbazones for treatment of **viral** and fungal infections)
- IT 412318-18-4P 412318-19-5P 412318-20-8P 412318-21-9P 412318-22-0P
412318-23-1P 412318-24-2P 412318-25-3P 412318-26-4P 412318-27-5P
412318-28-6P 412318-29-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aminopyridinecarboxyaldehyde thiosemicarbazones for treatment of **viral** and fungal infections)
- IT 126-07-8, Griseofulvin 154-17-6, 2-Deoxy-D-glucose 1397-89-3, Amphotericin B 1400-61-9, Nystatin 2398-96-1, Tolnaftate 3056-17-5 3416-05-5, 2',3'-Dideoxythymidine 4097-22-7, 2',3'-Dideoxyadenosine 4428-95-9, Foscarnet 7481-88-1 7481-89-2, 2',3'-Dideoxycytidine 11096-26-7, Erythropoietin 19130-96-2, 1-Deoxynojirimycin 23593-75-1, Clotrimazole 30516-87-1, AZT 36791-04-5, Ribavirin 38640-92-5, Ampligen 59277-89-3, Acyclovir 69558-55-0, Thymopentin 69655-05-6, 2',3'-Dideoxyinosine 79831-76-8, Castanospermine 82410-32-0, Gancyclovir 83869-56-1, GM-CSF 84625-61-6, Itraconazole 86386-73-4, Fluconazole 90803-92-2, Thymomodulin 91161-71-6, Terbinafine 134678-17-4, 3TC 135212-57-6 142340-99-6, Adefovir Dipivoxil 143621-35-6, Triapine 143621-35-6 **147058-39-7** 162808-62-0, Caspofungin 171228-49-2, Posaconazole 181785-84-2 202138-50-9
RL: **PAC (Pharmacological activity); THU (Therapeutic use);** BIOL (Biological study); USES (Uses)
(aminopyridinecarboxyaldehyde thiosemicarbazones for treatment of **viral** and fungal infections)
- IT 79-19-6, Hydrazinecarbothioamide 100-42-5, Styrene, reactions 2357-33-7 2916-68-9, 2-(Trimethylsilyl)ethanol 2942-59-8, 2-Chloronicotinic acid 5330-38-1 6641-02-7 22470-99-1 39224-61-8 41951-76-2 59648-29-2 64917-81-3 174264-62-1 174265-02-2 412318-90-2 412318-91-3

RL: RCT (Reactant); RACT (Reactant or reagent)
(aminopyridinecarboxyaldehyde thiosemicarbazones for treatment of
viral and fungal infections)

IT 14578-18-8P 40134-18-7P, 2-Chloronicotinic acid methyl ester
171360-37-5P 220257-04-5P 412318-30-0P 412318-31-1P 412318-32-2P
412318-33-3P 412318-34-4P 412318-35-5P 412318-36-6P 412318-37-7P
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412318-85-5P 412318-86-6P 412318-87-7P 412318-88-8P 412318-89-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(aminopyridinecarboxyaldehyde thiosemicarbazones for treatment of
viral and fungal infections)

IT 9068-38-6, Reverse transcriptase

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; aminopyridinecarboxyaldehyde thiosemicarbazones for
treatment of **viral** and fungal infections)

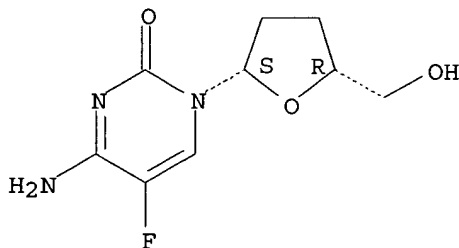
IT 147058-39-7

RL: **PAC (Pharmacological activity); THU (Therapeutic
use)**; BIOL (Biological study); USES (Uses)
(aminopyridinecarboxyaldehyde thiosemicarbazones for treatment of
viral and fungal infections)

RN 147058-39-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-
(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L34 ANSWER 19 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:555629 HCAPLUS

DOCUMENT NUMBER: 137:125359

TITLE: Preparation of nucleoside derivatives as inhibitors of
RNA-dependent RNA **viral** polymerase

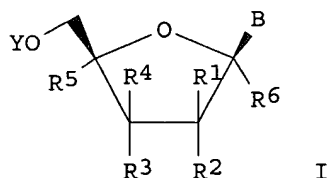
INVENTOR(S): Carroll, Steven S.; Lafemina, Robert L.; Hall, Dawn
L.; Himmelberger, Amy L.; Kuo, Lawrence C.; Maccoss,
Malcolm; Olsen, David B.; Rutkowski, Carrie A.;
Tomassini, Joanne E.; An, Haoyun; Bhat, Balkrishen;
Bhat, Neelima; Cook, Phillip Dan; Eldrup, Anne B.;
Guinosso, Charles J.; Prhavic, Marija; Prakash, Thazha
P.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Isis Pharmaceuticals, Inc.

SOURCE: PCT Int. Appl., 235 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002057425	A2	20020725	WO 2002-US1531	20020118
WO 2002057425	A3	20050421		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2433878	AA	20020725	CA 2002-2433878	20020118
US 2002147160	A1	20021010	US 2002-52318	20020118
US 6777395	B2	20040817		
CN 1498221	A	20040519	CN 2002-806977	20020118
JP 2004532184	T2	20041021	JP 2002-558479	20020118
EP 1539188	A2	20050615	EP 2002-709095	20020118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004072788	A1	20040415	US 2003-431657	20030507
ZA 2003005078	A	20040521	ZA 2003-5078	20030630
US 2004067901	A1	20040408	US 2003-688691	20031017
US 2004110717	A1	20040610	US 2004-250873	20040116
US 2005272676	A1	20051208	US 2005-200499	20050809
PRIORITY APPLN. INFO.:				
			US 2001-263313P	P 20010122
			US 2001-282069P	P 20010406
			US 2001-299320P	P 20010619
			US 2001-344528P	P 20011025
			US 2002-52318	A3 20020118
			WO 2002-US1531	W 20020118
			US 2003-431657	B1 20030507
OTHER SOURCE(S): MARPAT 137:125359				
GI				



AB The present invention provides the preparation of nucleoside compds. I, wherein B is nucleobase, Y is H, alkylcarbonyl, phosphate; R1 is H, alkenyl, alkynyl, alkyl; R2 and R3 are independently H, OH, halogen, alkyl, alkoxy, alkenyloxy, alkylthio, alkylcarbonyloxy, aryloxyrcbonyl, azido, amino, alkylamino; R1 and R2 together with the carbon atom to which they are attached form a 3- to 6-membered heterocycle; R4 is H, OH, SH, NH2,

alkylamino, cycloalkylamino, halogen, alkyl, alkoxy, CF₃; R₅ and R₆ are independently H, hydroxymethyl, Me, fluoromethyl; and certain derivs. thereof which are inhibitors of RNA-dependent RNA viral polymerase. These compds. are inhibitors of RNA-dependent RNA viral replication and are useful for the treatment of RNA-dependent RNA viral infection. They are particularly useful as inhibitors of **hepatitis C virus (HCV)** NS5B polymerase, as inhibitors of **HCV** replication, and/or for the treatment of **hepatitis C** infection. The invention also describes pharmaceutical compns. containing such nucleoside compds. alone or in combination with other agents active against RNA-dependent RNA viral infection, in particular **HCV** infection. Also disclosed are methods of inhibiting RNA-dependent RNA polymerase, inhibiting RNA-dependent RNA viral replication, and/or treating RNA-dependent RNA viral infection with the nucleoside compds. of the present invention. Thus, 4-amino-1-(2-C-methyl-β-D-ribofuranosyl)-1H-pyrazolo[3,4-d]pyrimidine was prepared as inhibitors of RNA-dependent RNA viral polymerase. Representative compds. tested in the **HCV** NS5B polymerase assay exhibited IC₅₀'s less than 100 μM. The compds. of the present invention were also evaluated for their ability to affect the replication of **Hepatitis C Virus** RNA in cultured hepatoma (HuH-7) cells containing a sub-genomic **HCV** Replicon.

IC ICM C12N

CC 33-9 (Carbohydrates)

Section cross-reference(s): 1, 7, 63

ST human cytotoxicity nucleoside prepn **antiviral hepatitis C**; cytotoxicity nucleoside prepn **antiviral hepatitis C**; nucleoside prepn inhibitor human RNA polymerase **antiviral hepatitis C**

IT **Antiviral agents**

Cytotoxicity

Fever and Hyperthermia

Hepatitis C virus

Human

Infection

(preparation of nucleoside derivs. as inhibitors of RNA-dependent human RNA **viral** polymerase)

IT RNA formation

(replication; preparation of nucleoside derivs. as inhibitors of RNA-dependent human RNA **viral** polymerase)

IT Infection

(**viral**; preparation of nucleoside derivs. as inhibitors of RNA-dependent human RNA **viral** polymerase)

IT 9026-28-2, RNA-dependent RNA Polymerase

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(**Hepatitis C Virus** NS5B; preparation of nucleoside derivs. as inhibitors of RNA-dependent human RNA **viral** polymerase)

IT 9026-93-1, Adenosine deaminase

RL: CAT (Catalyst use); USES (Uses)

(preparation of nucleoside derivs. as inhibitors of RNA-dependent human RNA **viral** polymerase)

IT 2140-72-9P, 2'-O-Methylcytidine 120401-36-7P

RL: IMF (Industrial manufacture); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of nucleoside derivs. as inhibitors of RNA-dependent human RNA **viral** polymerase)

IT	86-01-1P	147-94-4P	606-58-6P	961-07-9P	2004-07-1P	2140-71-8P
	2140-79-6P	2504-55-4P	2564-35-4P	2946-39-6P	3258-05-7P	
	3868-32-4P	3868-33-5P	4016-63-1P	4209-30-7P	6736-58-9P	
	7013-16-3P	10058-66-9P	13191-15-6P	14675-48-0P	15676-18-3P	
	16220-07-8P	17210-68-3P	17434-81-0P	18417-89-5P	20724-73-6P	
	22423-10-5P	23197-98-0P	23567-96-6P	23567-97-7P	24121-00-4P	
	24909-13-5P	26383-05-1P	26889-39-4P	26889-42-9P	28072-46-0P	
	28072-49-3P	30948-06-2P	35874-49-8P	38819-10-2P	40725-89-1P	
	55968-37-1P	56039-11-3P	61210-21-7P	61468-90-4P	61556-44-3P	
	62160-23-0P	64183-27-3P	64526-34-7P	65114-35-4P	65444-12-4P	
	68345-70-0P	69199-40-2P	69383-05-7P	70932-91-1P	72490-81-4P	
	73449-07-7P	76617-73-7P	78153-66-9P	78842-13-4P	79816-01-6P	
	80791-87-3P	83379-31-1P	84017-61-8P	86392-75-8P	87202-41-3P	
	88970-14-3P	93366-96-2P	101212-50-4P	101515-08-6P	103122-85-6P	
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	123402-25-5P	123402-27-7P	136208-63-4P	139209-26-0P	141232-24-8P	
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	175787-23-2P	181356-39-8P	199859-58-0P	202186-97-8P	215942-59-9P	
	262417-55-0P	317820-43-2P	318247-10-8P	355805-46-8P	355805-55-9P	
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	444019-23-2P	444019-25-4P	444019-27-6P	444019-29-8P		
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	444019-48-1P	444019-49-2P	444019-50-5P	444019-51-6P	444019-52-7P	
	444019-53-8P	444019-54-9P	444019-55-0P	444019-56-1P	444019-57-2P	
	444019-58-3P	444019-59-4P	444019-60-7P	444019-61-8P	444019-62-9P	
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	444019-73-2P	444019-74-3P	444019-75-4P	444019-76-5P	444019-77-6P	
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	444019-83-4P	444019-84-5P	444019-87-8P	444019-99-2P	444020-04-6P	
	444020-09-1P	444020-20-6P	444020-25-1P	444020-48-8P	444020-62-6P	
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	444020-72-8P	444020-73-9P	444020-74-0P	444020-75-1P	444020-76-2P	
	444020-77-3P	444020-78-4P	444020-79-5P	444020-80-8P	444020-81-9P	
	444020-82-0P	444020-83-1P	444020-84-2P	444020-85-3P	444020-86-4P	
	444020-87-5P	444020-88-6P	444020-89-7P			

RL: IMF (Industrial manufacture); **PAC (Pharmacological activity)**

; SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL

(Biological study); PREP (Preparation); USES (Uses)

(preparation of nucleoside derivs. as inhibitors of RNA-dependent human RNA viral polymerase)

IT	444020-90-0P	444020-91-1P	444020-92-2P	444020-93-3P	444020-94-4P
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	444021-15-2P	444021-16-3P	444021-17-4P	444021-18-5P	444021-19-6P
	444021-20-9P	444021-21-0P	444021-22-1P	444021-23-2P	444021-24-3P

444021-25-4P	444021-28-7P	444021-29-8P	444021-30-1P	444021-31-2P
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444021-37-8P	444021-38-9P	444021-39-0P	444021-40-3P	444021-41-4P
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444021-49-2P	444021-52-7P	444021-55-0P	444021-58-3P	444021-60-7P
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444021-69-6P	444021-70-9P	444021-71-0P	444021-72-1P	444021-73-2P
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444022-24-6P	444022-25-7P			

RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of nucleoside derivs. as inhibitors of RNA-dependent human RNA viral polymerase)

IT	90213-73-3P	90213-74-4P	115479-40-8P	115479-42-0P	161110-12-9P
	161169-94-4P	168427-35-8P	168777-53-5P	168777-55-7P	212061-24-0P
	212061-25-1P	312934-29-5P	312934-35-3P	312934-48-8P	317820-41-0P
	318246-85-4P	318246-92-3P	318247-02-8P	443642-30-6P	443642-31-7P
	443642-32-8P	443642-33-9P	443642-35-1P	443642-36-2P	443642-37-3P
	443642-39-5P	443642-40-8P	443642-50-0P	443642-51-1P	443642-52-2P
	443642-54-4P	443642-55-5P	443642-58-8P	443642-61-3P	443642-64-6P
	443642-68-0P	443642-69-1P	443642-70-4P	443642-71-5P	443642-72-6P
	443642-73-7P	443642-75-9P	443642-77-1P	443642-78-2P	443642-79-3P
	443642-84-0P	443642-85-1P	443642-90-8P	443642-91-9P	443642-92-0P
	443642-93-1P	443642-94-2P	444018-77-3P	444018-78-4P	444018-80-8P
	444018-82-0P	444018-83-1P	444018-84-2P	444018-86-4P	444018-87-5P
	444018-89-7P	444018-93-3P	444018-95-5P	444018-98-8P	444019-01-6P
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	444019-26-5P	444019-28-7P	444019-31-2P	444019-32-3P	444019-33-4P
	444019-34-5P	444019-35-6P	444019-36-7P	444019-37-8P	444019-38-9P
	444019-85-6P	444019-86-7P	444019-88-9P	444020-01-3P	

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of nucleoside derivs. as inhibitors of RNA-dependent human RNA viral polymerase)

IT 160526-82-9P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of nucleoside derivs. as inhibitors of RNA-dependent human RNA viral polymerase)

IT 94-99-5 872-50-4, 1-Methyl-2-pyrrolidinone, uses

RL: NUU (Other use, unclassified); USES (Uses)

(preparation of nucleoside derivs. as inhibitors of RNA-dependent human RNA viral polymerase)

IT 60-24-2, 2-Mercaptoethanol 69-33-0, Tubercidin 124-07-2, Octanoic acid, reactions 524-38-9, N-Hydroxyphthalimide 937-14-4, 3-Chloroperbenzoic acid 1618-36-6 2096-10-8, 2-Aminoadenosine 2380-63-4, 1H-Pyrazolo[3,4-d]pyrimidin-4-amine 3680-69-1 7057-33-2, 3'-Deoxycytidine 15397-12-3 18422-43-0 19393-83-0 40635-67-4, α -Acetoxyisobutyryl bromide 56039-06-6 68703-51-5 70384-51-9

79159-76-5 84955-31-7 85335-76-8 90358-16-0 102690-94-8
 102731-45-3 127047-59-0 129786-41-0 153121-88-1 168427-36-9
 171763-19-2 177414-97-0 213623-59-7 318246-79-6 443642-59-9
 443642-76-0 444018-75-1 444018-91-1 444018-94-4 444018-97-7
 444019-00-5 444019-07-2 444019-11-8 444019-14-1 444019-16-3
 444019-18-5 444019-20-9 444019-22-1 444019-24-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of nucleoside derivs. as inhibitors of RNA-dependent human RNA
viral polymerase)

IT 9012-90-2, DNA polymerase

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (α , β , and γ human; preparation of nucleoside derivs. as
 inhibitors of RNA-dependent human RNA **viral** polymerase)

IT 444019-25-4P

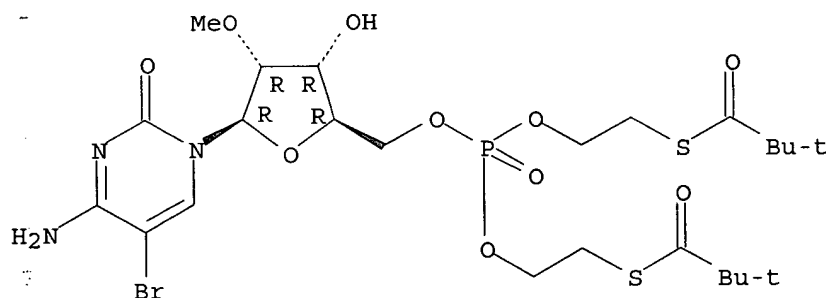
RL: IMF (Industrial manufacture); **PAC (Pharmacological activity)**
 ; SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL
 (Biological study); PREP (Preparation); USES (Uses)

(preparation of nucleoside derivs. as inhibitors of RNA-dependent human RNA
viral polymerase)

RN 444019-25-4 HCAPLUS

CN 5'-Cytidylic acid, 5-bromo-2'-O-methyl-, bis[2-[(2,2-dimethyl-1-
 oxopropyl)thio]ethyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L34 ANSWER 20 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:314958 HCAPLUS

DOCUMENT NUMBER: 136:340939

TITLE: Preparation of modified nucleosides for treatment of
viral infections and abnormal cellular
 proliferation

INVENTOR(S): Stuyver, Lieven; Watanabe, Kyoichi A.

PATENT ASSIGNEE(S): Pharmasset Limited, USA

SOURCE: PCT Int. Appl., 230 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

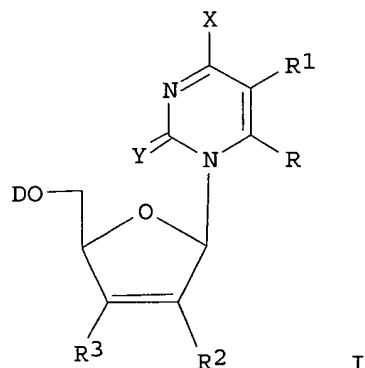
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002032920	A2	20020425	WO 2001-US46113	20011018
WO 2002032920	A3	20040219		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
 HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
 LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
 RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
 VN, YU, ZA, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG,
 KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR,
 IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
 GQ, GW, ML, MR, NE, SN, TD, TG
 CA 2426187 AA 20020425 CA 2001-2426187 20011018
 AU 2002028749 A5 20020429 AU 2002-28749 20011018
 US 2003087873 A1 20030508 US 2001-45292 20011018
 EP 1411954 A2 20040428 EP 2001-987756 20011018
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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 JP 2004533406 T2 20041104 JP 2002-536301 20011018
 CN 1646141 A 20050727 CN 2001-820816 20011018
 BR 2001014837 A 20060509 BR 2001-14837 20011018
 PRIORITY APPLN. INFO.: US 2000-241488P P 20001018
 US 2001-282156P P 20010406
 WO 2001-US46113 W 20011018

OTHER SOURCE(S): MARPAT 136:340939
 GI



AB Modified nucleosides, e.g. I, wherein D is hydrogen, alkyl, acyl, monophosphate, diphosphate, triphosphate, monophosphate ester, diphosphate ester, triphosphate ester, phospholipid or amino acid; X is H, halogen, NH₂, substituted amine, oxime, OH, alkoxy, SH, thioalkyl; Y is O, S, Se; R and R₁ are independently H, alkyl, alkenyl, alkynyl, aryl, alkylaryl, halogen, NH₂, substituted amine, oxime, hydrazine, OH, alkoxy, SH, thioalkyl, NO₂, NO, CH₂OH, CH₂OH, ester, CONH₂, amide, CN; R₂ and R₃ are independently H, halogen, OH, SH, OMe, SMe, NH₂, NHMe, CH:CH₂, CN, CH₂NH₂, CH₂OH, CO₂H; were prepared for treating a Flaviviridae (including BVDV and HCV), Orthomyxoviridae (including Influenza A and B) or Paramyxoviridae (including RSV) infection, or conditions related to abnormal cellular proliferation, in a host, including animals, and especially humans. This invention also provides an effective process to quantify the viral load, and in particular BVDV, HCV or West Nile Virus load, in a host, using real-time polymerase chain reaction ("TR-PCR"). Addnl., the invention discloses probe mols. that can fluoresce proportionally to the amount of virus present in a sample. Thus, (1'R,2'S,3'R,4'R)-1-[2,3-dihydroxy-4-(hydroxymethyl)cyclopentan-1-yl]-5-fluorocytosine was prepared

and tested in vitro as **antiviral** and antitumor agent.

IC ICM C07H019-00

CC 33-9 (Carbohydrates)

Section cross-reference(s): 1, 7, 10, 63

ST cytotoxicity nucleoside prepn **antiviral** antitumor human antiinfluenza; polymerase chain reaction nucleoside prepn **antiviral** antitumor human antiinfluenza; nucleoside prepn **antiviral** antitumor human antiinfluenza Orthomyxoviridae Paramyxoviridae Flaviviridae

IT Antitumor agents

Antiviral agents

Cytotoxicity

Human

PCR (polymerase chain reaction)

West Nile virus

(preparation of modified nucleosides for treatment of **viral** infections and abnormal cellular proliferation)

IT Nucleosides, preparation

RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of modified nucleosides for treatment of **viral** infections and abnormal cellular proliferation)

IT Bovine diarrhea virus

Flaviviridae

Hepatitis C virus

Influenza A virus

Influenza B virus

Orthomyxoviridae

Paramyxoviridae

(treatment; preparation of modified nucleosides for treatment of **viral** infections and abnormal cellular proliferation)

IT Infection

(**viral**, treatment; preparation of modified nucleosides for treatment of **viral** infections and abnormal cellular proliferation)

IT 50-91-9P 73-03-0P 131-06-6P 147-94-4P 316-46-1P 727-79-7P

957-77-7P 1445-07-4P 1826-95-5P 1868-36-6P 2096-10-8P 2133-80-4P

2341-22-2P 3066-86-2P 3080-29-3P 4097-22-7P

4298-10-6P 5399-87-1P 6554-11-6P 6982-08-7P 7057-48-9P

10212-18-7P 10212-19-8P 10212-22-3P 13491-41-3P 13491-43-5P

13491-46-8P 13491-47-9P 13957-31-8P **17676-66-3P**

18427-02-6P **18829-84-0P** 23899-77-6P 27921-78-4P

32791-81-4P 40632-26-6P 42867-68-5P 42867-78-7P 53766-80-6P

57100-18-2P 57729-40-5P 58461-29-3P 58461-30-6P **58461-34-0P**

60301-51-1P 60786-47-2P 60786-48-3P 60786-49-4P 61037-75-0P

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67036-65-1P 69321-95-5P 70421-27-1P 71184-20-8P 72877-50-0P

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415705-72-5P 415705-73-6P 415705-74-7P 415705-75-8P 415705-77-0P

RL: IMF (Industrial manufacture); PAC (Pharmacological activity)

; SPN (Synthetic preparation); THU (Therapeutic use); BIOL

(Biological study); PREP (Preparation); USES (Uses)

(preparation of modified nucleosides for treatment of viral
infections and abnormal cellular proliferation)

IT 415705-78-1P 415705-79-2P 415705-80-5P 415705-81-6P 415705-82-7P
415705-83-8P 415705-84-9P 415705-85-0P 415705-86-1P 415705-87-2P
415705-88-3P 415705-89-4P 415705-90-7P 415705-92-9P 415705-94-1P
415705-96-3P 415705-97-4P 415705-98-5P 415705-99-6P 415706-00-2P
415706-01-3P 415707-26-5P 415707-27-6P 415707-28-7P 415927-02-5P
415927-03-6P 415927-04-7P

RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN
(Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
PREP (Preparation); USES (Uses)

(preparation of modified nucleosides for treatment of viral
infections and abnormal cellular proliferation)

IT 2627-64-7P 3258-02-4P 3803-28-9P 4710-75-2P 7057-27-4P
7057-33-2P 14057-25-1P 18829-83-9P 22855-06-7P 24514-26-9P
25383-84-0P 37731-72-9P 38642-28-3P 52482-84-5P 52482-85-6P
54937-38-1P 56889-16-8P 67036-63-9P 114861-14-2P 128496-21-9P
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415704-37-9P 415704-38-0P 415704-40-4P 415704-41-5P 415704-43-7P
415704-44-8P 415704-45-9P 415704-46-0P 415704-47-1P 415704-48-2P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic
preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of modified nucleosides for treatment of viral
infections and abnormal cellular proliferation)

IT 51-21-8, 5-Fluorouracil 58-61-7, Adenosine, reactions 58-96-8, Uridine
65-71-4, Thymine 87-42-3, 6-Chloropurine 1005-56-7, Phenyl

chlorothionoformate 3106-03-4, 5-Nitrouridine 3768-18-1 5432-33-7
6553-96-4, 2,4,6-Triisopropylbenzenesulfonyl chloride 10526-27-9
20031-21-4 42927-46-8 128114-98-7 223596-25-6 415704-42-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of modified nucleosides for treatment of **viral**
infections and abnormal cellular proliferation)

IT 417196-37-3 417196-38-4 417196-39-5 417196-40-8 417196-41-9
417196-42-0

RL: PRP (Properties)

(unclaimed sequence; preparation of modified nucleosides for treatment of
viral infections and abnormal cellular proliferation)

IT 2341-22-2P 3066-86-2P 4298-10-6P
17676-66-3P 18829-84-0P 58461-34-0P
67036-59-3P 67036-61-7P 83966-93-2P
374107-80-9P 415704-64-2P 415704-65-3P
415704-66-4P 415704-67-5P 415704-68-6P
415704-69-7P 415704-70-0P 415704-71-1P
415704-72-2P 415704-73-3P 415704-74-4P
415704-75-5P 415704-76-6P 415704-77-7P
415704-78-8P 415704-79-9P 415704-80-2P
415704-81-3P 415704-82-4P 415704-83-5P
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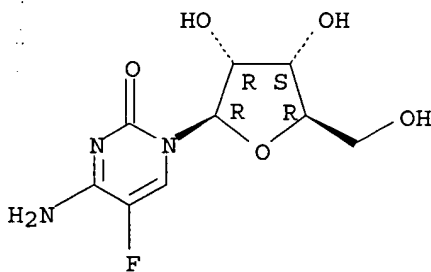
RL: IMF (Industrial manufacture); PAC (Pharmacological activity)
; SPN (Synthetic preparation); THU (Therapeutic use); BIOL
(Biological study); PREP (Preparation); USES (Uses)

(preparation of modified nucleosides for treatment of **viral**
infections and abnormal cellular proliferation)

RN 2341-22-2 HCAPLUS

CN Cytidine, 5-fluoro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

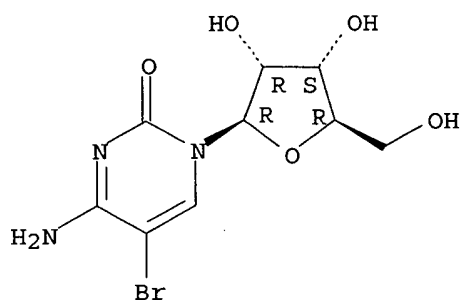
Absolute stereochemistry.



RN 3066-86-2 HCAPLUS

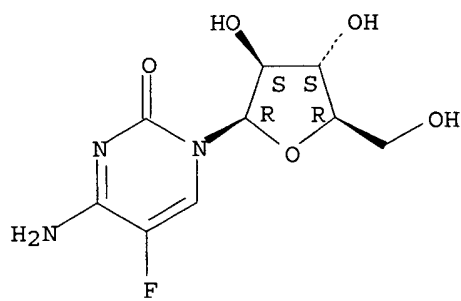
CN Cytidine, 5-bromo- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



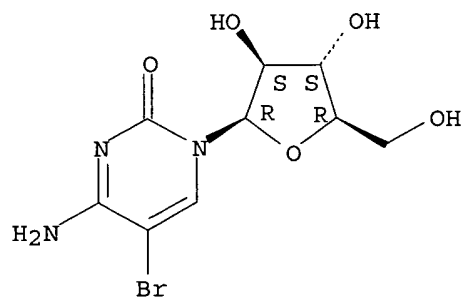
RN 4298-10-6 HCAPLUS
CN 2(1H)-Pyrimidinone, 4-amino-1-β-D-arabinofuranosyl-5-fluoro- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



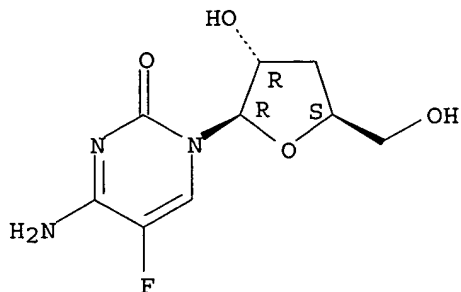
RN 17676-66-3 HCAPLUS
CN 2(1H)-Pyrimidinone, 4-amino-1-β-D-arabinofuranosyl-5-bromo- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



RN 18829-84-0 HCAPLUS
CN Cytidine, 3'-deoxy-5-fluoro- (8CI, 9CI) (CA INDEX NAME)

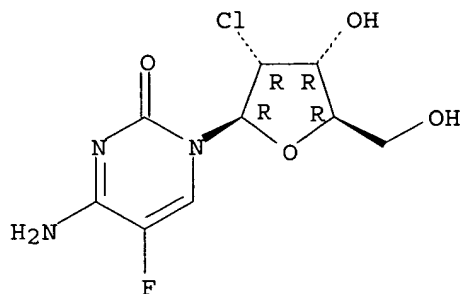
Absolute stereochemistry.



RN 58461-34-0 HCAPLUS

CN Cytidine, 2'-chloro-2'-deoxy-5-fluoro- (9CI) (CA INDEX NAME)

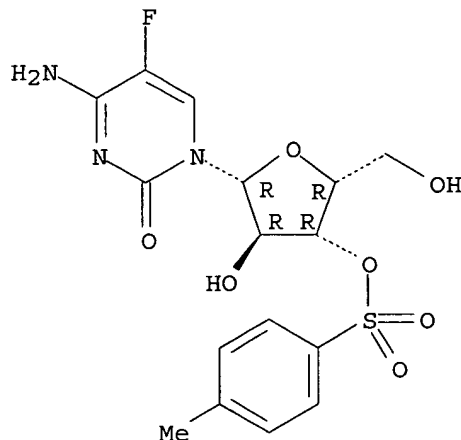
Absolute stereochemistry.



RN 67036-59-3 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[3-O-[(4-methylphenyl)sulfonyl]-β-D-xylofuranosyl]- (9CI) (CA INDEX NAME)

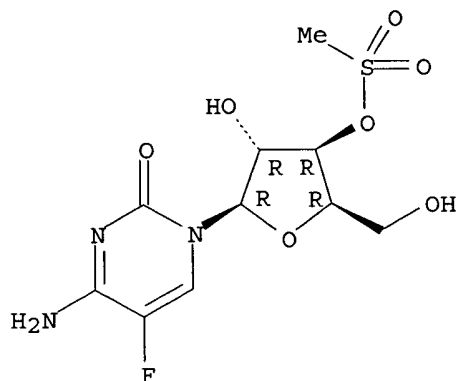
Absolute stereochemistry.



RN 67036-61-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[3-O-(methylsulfonyl)-β-D-xylofuranosyl]- (9CI) (CA INDEX NAME)

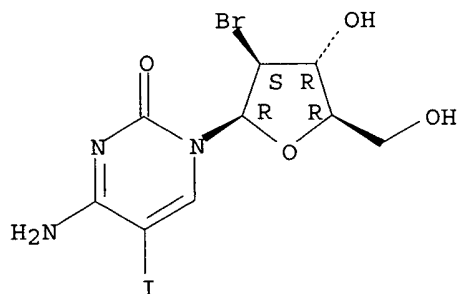
Absolute stereochemistry.



RN 83966-93-2 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-bromo-2-deoxy-β-D-arabinofuranosyl)-5-iodo- (9CI) (CA INDEX NAME)

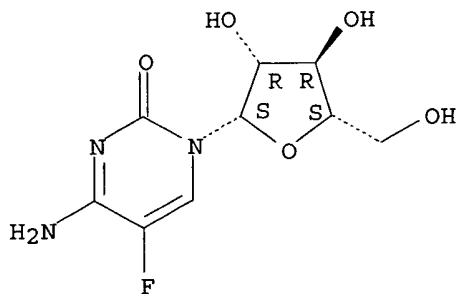
Absolute stereochemistry.



RN 374107-80-9 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-β-L-arabinofuranosyl-5-fluoro- (9CI) (CA INDEX NAME)

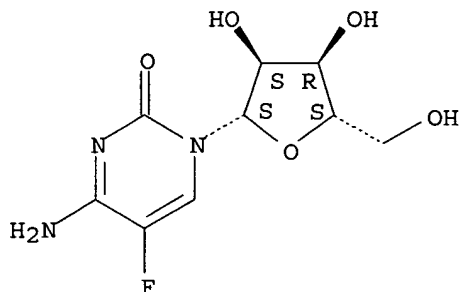
Absolute stereochemistry. Rotation (-).



RN 415704-64-2 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-β-L-ribofuranosyl- (9CI) (CA INDEX NAME)

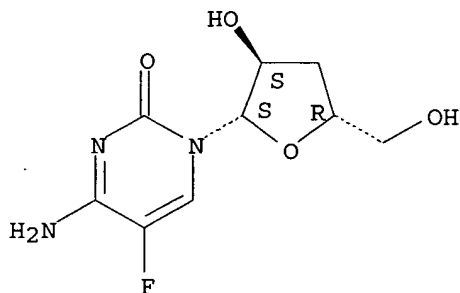
Absolute stereochemistry.



RN 415704-65-3 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(3-deoxy-β-L-erythro-pentofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

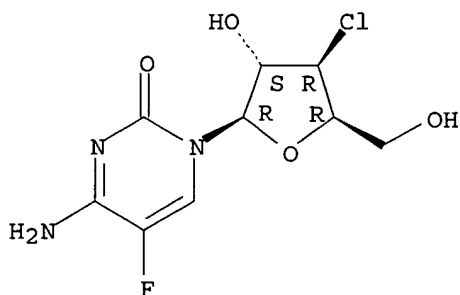
Absolute stereochemistry.



RN 415704-66-4 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(3-chloro-3-deoxy-β-D-xylofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

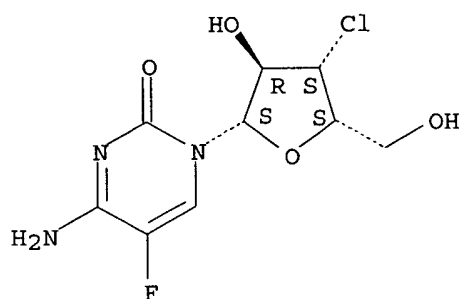
Absolute stereochemistry.



RN 415704-67-5 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(3-chloro-3-deoxy-β-L-xylofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

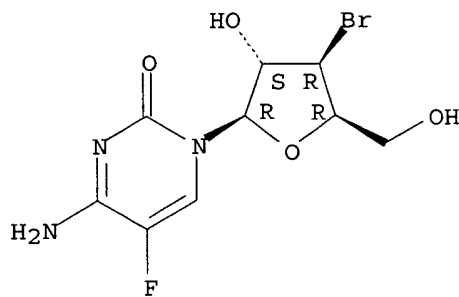
Absolute stereochemistry.



RN 415704-68-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(3-bromo-3-deoxy-β-D-xylofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

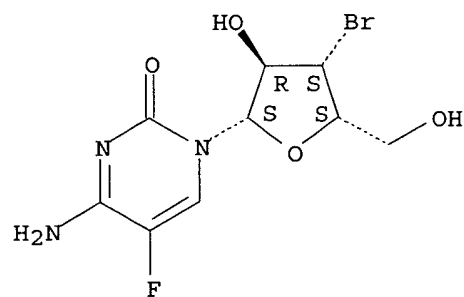
Absolute stereochemistry.



RN 415704-69-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(3-bromo-3-deoxy-β-L-xylofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

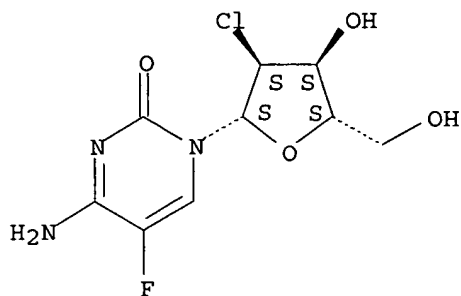
Absolute stereochemistry.



RN 415704-70-0 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-chloro-2-deoxy-β-L-ribofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

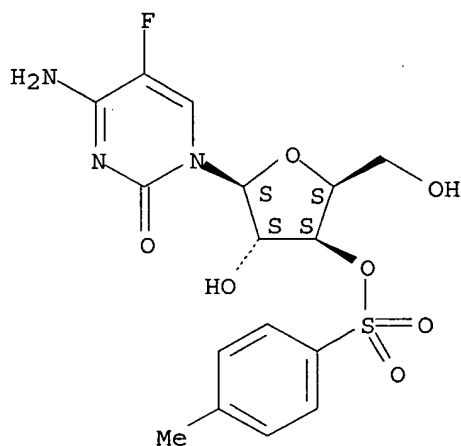
Absolute stereochemistry.



RN 415704-71-1 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[3-O-[(4-methylphenyl)sulfonyl]-β-L-xylofuranosyl]- (9CI) (CA INDEX NAME)

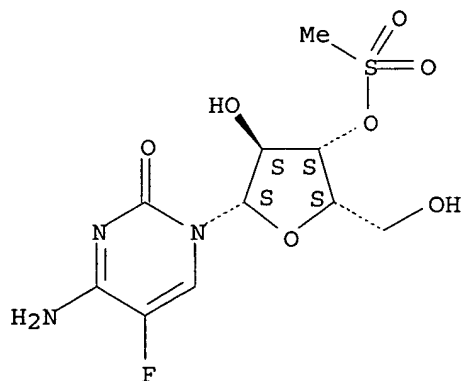
Absolute stereochemistry.



RN 415704-72-2 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[3-O-(methylsulfonyl)-β-L-xylofuranosyl]- (9CI) (CA INDEX NAME)

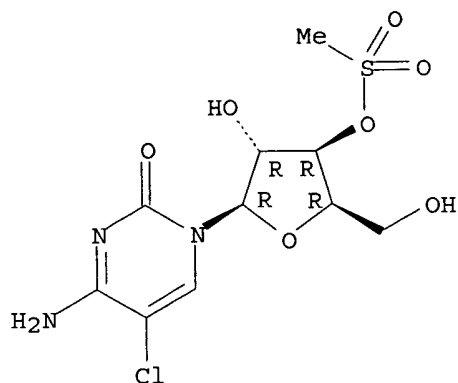
Absolute stereochemistry.



RN 415704-73-3 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-chloro-1-[3-O-(methylsulfonyl)- β -D-xylofuranosyl]- (9CI) (CA INDEX NAME)

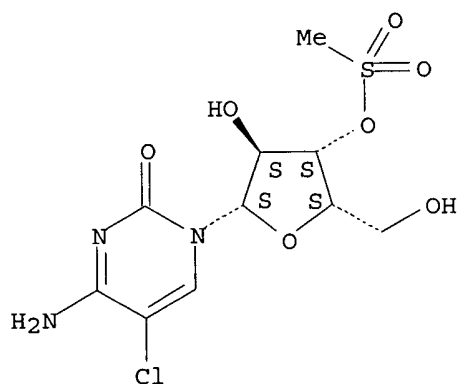
Absolute stereochemistry.



RN 415704-74-4 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-chloro-1-[3-O-(methylsulfonyl)- β -L-xylofuranosyl]- (9CI) (CA INDEX NAME)

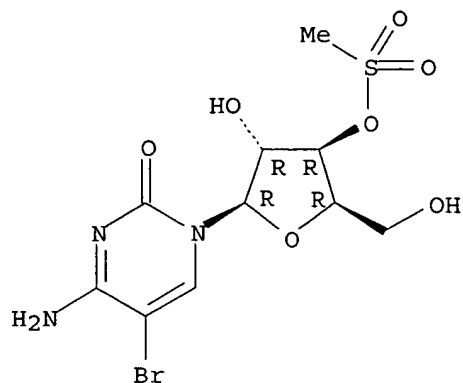
Absolute stereochemistry.



RN 415704-75-5 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-bromo-1-[3-O-(methylsulfonyl)- β -D-xylofuranosyl]- (9CI) (CA INDEX NAME)

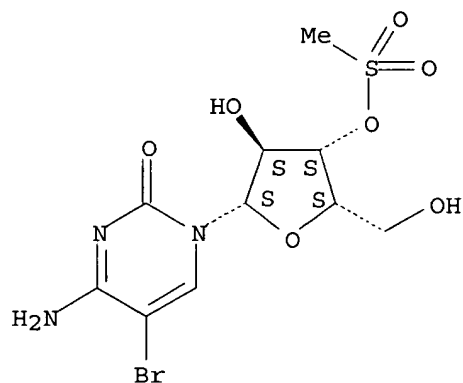
Absolute stereochemistry.



RN 415704-76-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-bromo-1-[3-O-(methylsulfonyl)-β-L-xylofuranosyl]- (9CI) (CA INDEX NAME)

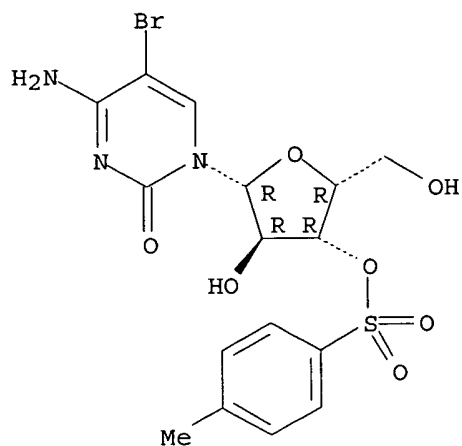
Absolute stereochemistry.



RN 415704-77-7 HCAPLUS

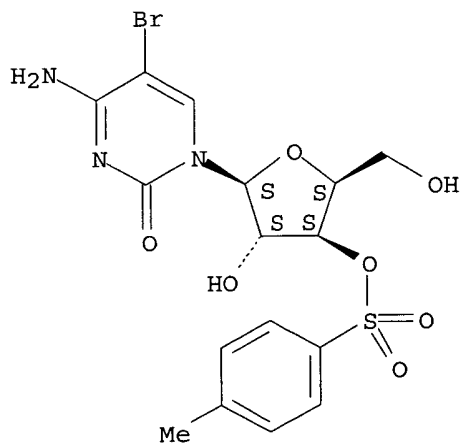
CN 2(1H)-Pyrimidinone, 4-amino-5-bromo-1-[3-O-[(4-methylphenyl)sulfonyl]-β-D-xylofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



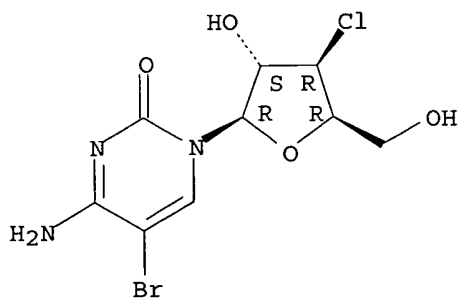
RN 415704-78-8 HCAPLUS
 CN 2(1H)-Pyrimidinone, 4-amino-5-bromo-1-[3-O-[(4-methylphenyl)sulfonyl]-
 β-L-xylofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 415704-79-9 HCAPLUS
 CN 2(1H)-Pyrimidinone, 4-amino-5-bromo-1-(3-chloro-3-deoxy-β-D-
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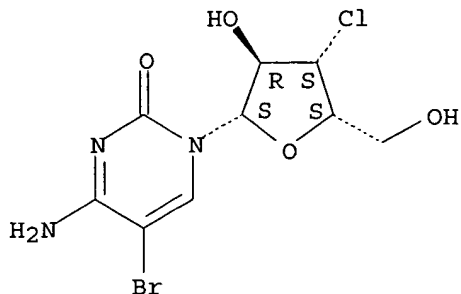
Absolute stereochemistry.



RN 415704-80-2 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-bromo-1-(3-chloro-3-deoxy- β -L-xylofuranosyl)- (9CI) (CA INDEX NAME)

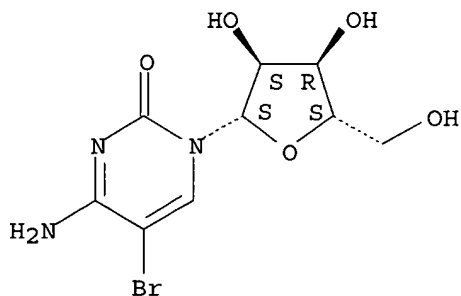
Absolute stereochemistry.



RN 415704-81-3 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-bromo-1- β -L-ribofuranosyl- (9CI) (CA INDEX NAME)

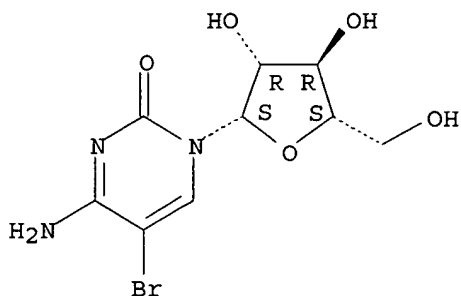
Absolute stereochemistry.



RN 415704-82-4 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1- β -L-arabinofuranosyl-5-bromo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

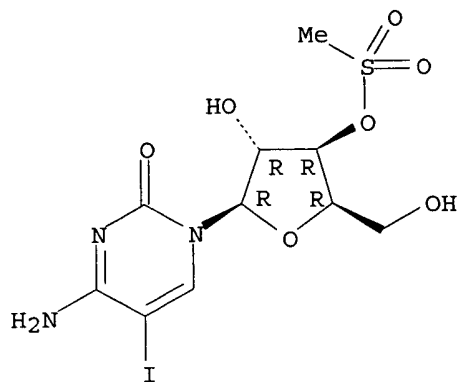


RN 415704-83-5 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-iodo-1-[3-O-(methylsulfonyl)- β -D-

xylofuranosyl]- (9CI) (CA INDEX NAME)

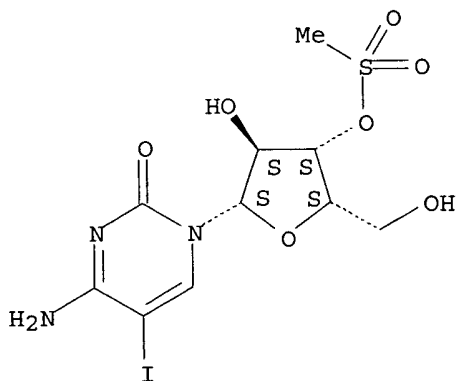
Absolute stereochemistry.



RN 415704-84-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-iodo-1-[3-O-(methylsulfonyl)-β-L-xylofuranosyl]- (9CI) (CA INDEX NAME)

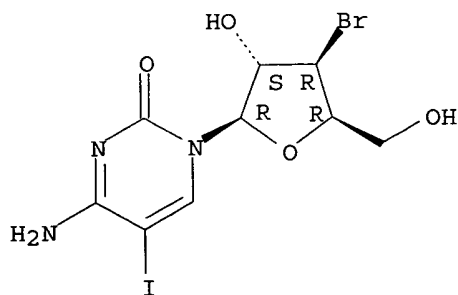
Absolute stereochemistry.



RN 415704-85-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(3-bromo-3-deoxy-β-D-xylofuranosyl)-5-iodo- (9CI) (CA INDEX NAME)

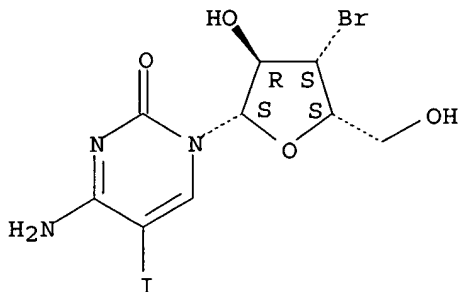
Absolute stereochemistry.



RN 415704-86-8 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(3-bromo-3-deoxy- β -L-xylofuranosyl)-5-iodo- (9CI) (CA INDEX NAME)

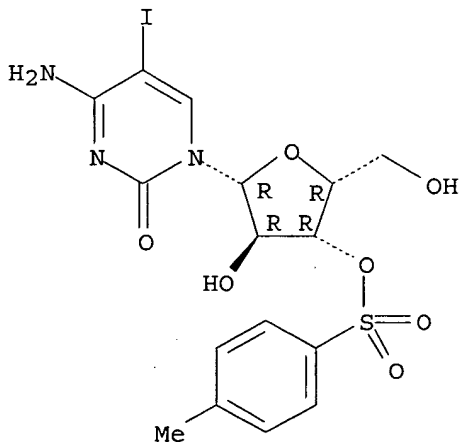
Absolute stereochemistry.



RN 415704-87-9 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-iodo-1-[3-O-[(4-methylphenyl)sulfonyl]- β -D-xylofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

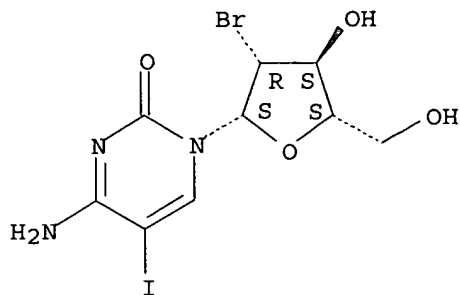


RN 415704-88-0 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-iodo-1-[3-O-[(4-methylphenyl)sulfonyl]- β -L-xylofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.



L34 ANSWER 21 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:171918 HCAPLUS

DOCUMENT NUMBER: 136:217007

TITLE: Preparation of **antiviral** nucleoside derivatives as inhibitors of subgenomic **hepatitis C virus** RNA replication

INVENTOR(S): Devos, Rene; Dymock, Brian William; Hobbs, Christopher John; Jiang, Wen-rong; Martin, Joseph Armstrong; Merrett, John Herbert; Najera, Isabel; Shimma, Nobuo; Tsukuda, Takuo

PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.

SOURCE: PCT Int. Appl., 225 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

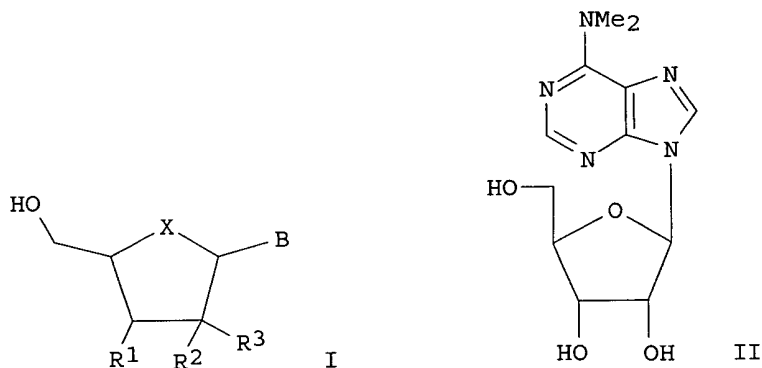
PATENT INFORMATION:

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WO 2002018404	C2	20031002		
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US 2003008841	A1	20030109	US 2001-923620	20010807
CA 2419399	AA	20020307	CA 2001-2419399	20010821
AU 2001095497	A5	20020313	AU 2001-95497	20010821
EP 1315736	A2	20030604	EP 2001-976128	20010821
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001013611	A	20030624	BR 2001-13611	20010821
JP 2004513083	T2	20040430	JP 2002-523918	20010821
ZA 2003001540	A	20040621	ZA 2003-1540	20030225
US 2004110718	A1	20040610	US 2003-678804	20031003

PRIORITY APPLN. INFO.:

GB 2000-21285	A 20000830
GB 2000-26611	A 20001031
US 2001-923620	B1 20010807
WO 2001-EP9633	W 20010821

OTHER SOURCE(S): MARPAT 136:217007
GI



AB Nucleosides I, wherein R1 is hydrogen, hydroxy, alkyl, hydroxyalkyl, alkoxy, halogen, cyano, isocyano or azido; R2 is hydrogen, hydroxy, alkoxy, chlorine, bromine or iodine; R3 is hydrogen; or R2 and R3 together represent =CH₂; or R2 and R3 represent fluorine; X is O, S or CH₂; B is a substituted purine base, were prepared as inhibitors of subgenomic **hepatitis C virus (HCV)** RNA replication. Thus, nucleoside II was prepared and tested for the inhibition of **HCV** RNA replication (EC₅₀ = 0.6 μM).

IC ICM C07H019-00

CC 33-9 (Carbohydrates)

Section cross-reference(s): 1, 63

ST human drug nucleoside prepn **antiviral** inhibitor **hepatitis C virus**; nucleoside prepn **antiviral** inhibitor **hepatitis C virus** RNA replication

IT **Antiviral** agents

Drugs

Hepatitis C virus

Human

(preparation of **antiviral** nucleoside derivs. as inhibitors of subgenomic **hepatitis C virus** RNA replication)

IT Nucleosides, preparation

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of **antiviral** nucleoside derivs. as inhibitors of subgenomic **hepatitis C virus** RNA replication)

IT RNA formation

(replication; preparation of **antiviral** nucleoside derivs. as inhibitors of subgenomic **hepatitis C virus** RNA replication)

IT 50-91-9P 131-06-6P 146-77-0P 550-33-4P 574-25-4P 605-23-2P
727-79-7P 957-75-5P 1463-10-1P 2096-10-8P 2104-65-6P 2139-60-8P

2140-61-6P 2140-69-4P 2140-76-3P 2248-74-0P 2341-22-2P
 2880-89-9P 2968-28-7P 3052-06-0P 3258-02-4P 3370-69-2P
 3530-56-1P 3768-18-1P 4016-63-1P 4298-10-6P 4338-48-1P
 4348-54-3P 4753-02-0P 4984-80-9P 5059-59-6P 5746-29-2P
 6220-32-2P 7057-33-2P 7084-29-9P 7481-89-2P 10578-79-7P
 13389-13-4P 13389-14-5P 13389-15-6P 13406-52-5P 13491-41-3P
 13957-31-8P 14357-08-5P 14985-44-5P 15763-12-9P 15824-83-6P
 17270-22-3P 17270-23-4P 17270-24-5P 20315-90-6P 21082-30-4P
 21967-06-6P 23605-76-7P 23707-33-7P 24723-77-1P 25110-76-3P
 26524-60-7P, L-Cytidine 26563-01-9P 26879-47-0P 34218-77-4P
 36396-99-3P 36799-20-9P 36799-21-0P 36799-22-1P 38594-97-7P
 38971-55-0P 40615-14-3P 40896-56-8P 41552-92-5P 41552-94-7P
 41552-95-8P 42870-41-7P 42870-55-3P 43138-95-0P 43138-97-2P
 43139-02-2P 43139-11-3P 43139-12-4P 49555-43-3P 52940-48-4P
 55652-72-7P 55677-94-6P 59856-78-9P 59856-80-3P 62805-43-0P
 65456-83-9P 65456-86-2P 66323-42-0P 67005-97-4P 69730-25-2P
 70020-72-3P 71118-23-5P 72959-69-4P 82448-44-0P 84765-98-0P
 86996-91-0P 87515-42-2P 95058-81-4P 95468-92-1P 95523-13-0P
 97826-35-2P 97826-58-9P 101565-57-5P 101565-65-5P 101565-79-1P
 101565-96-2P 121154-57-2P 121456-55-1P 121637-32-9P 125217-37-0P
 129885-95-6P 133713-59-4P 136003-97-9P 153381-14-7P 161686-49-3P
 161686-50-6P 165546-13-4P 220522-96-3P 220522-97-4P 236755-49-0P
 260365-30-8P 265988-77-0P 279670-35-8P 279670-38-1P
 279670-39-2P 279670-40-5P 279670-41-6P 279670-43-8P 309253-78-9P
 352025-67-3P 352025-69-5P 352025-74-2P 355134-58-6P 402724-29-2P
 402724-30-5P 402724-31-6P 402724-32-7P 402724-33-8P 402724-38-3P
 402724-39-4P 402724-40-7P 402724-41-8P 402724-42-9P 402724-43-0P
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 402724-54-3P 402724-55-4P 402724-56-5P 402724-57-6P 402724-58-7P
 402724-59-8P 402724-60-1P 402724-62-3P 402724-63-4P 402724-64-5P
 402724-65-6P 402724-67-8P 402724-70-3P 402724-71-4P 402724-72-5P
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 402724-78-1P 402724-80-5P 402724-81-6P 402724-82-7P 402724-83-8P
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 402725-10-4P 402725-11-5P 402725-12-6P 402725-13-7P 402725-14-8P
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 402725-47-7P 402725-48-8P 402725-49-9P 402725-50-2P 402725-51-3P
 402725-52-4P 402725-53-5P 402725-54-6P 402725-55-7P 402725-56-8P
 402725-57-9P 402725-58-0P 402725-59-1P 402725-60-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation);

THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)

(preparation of **antiviral** nucleoside derivs. as inhibitors of
subgenomic **hepatitis C virus** RNA
replication)

IT 146-92-9 316-46-1, 5-Fluorouridine 342-69-8 2620-62-4 2946-39-6
5399-87-1

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(preparation of **antiviral** nucleoside derivs. as inhibitors of
subgenomic **hepatitis C virus** RNA
replication)

IT 58-61-7, Adenosine, reactions 66-22-8, Uracil, reactions 73-03-0

76-83-5, Chlorotriphenylmethane 98-80-6, Phenylboronic acid 102-09-0,
 Diphenyl carbonate 111-49-9 123-75-1, Pyrrolidine, reactions
 123-90-0, Thiomorpholine 288-88-0, 1H-1,2,4-Triazole 627-35-0,
 N-Methylpropylamine 627-37-2, N-Methylallylamine 696-59-3,
 2,5-Dimethoxytetrahydrofuran 1904-98-9, 2,6-Diaminopurine 1928-89-8
 3056-18-6 3083-77-0 3181-38-2 3736-77-4 4212-49-1, 5-Ethyluracil
 5382-16-1, 4-Hydroxypiperidine 5536-17-4 5987-73-5 6165-69-1,
 Thiophene-3-boronic acid 6974-32-9 10310-21-1, 2-Amino-6-chloropurine
 14215-97-5 15176-29-1 20125-39-7 26287-72-9 29851-57-8
 30516-87-1, 3'-Azido-3'-deoxythymidine 35161-71-8, N-
 Methylpropargylamine 55627-73-1, 8-Bromoinosine 64911-28-0
 90813-55-1 129885-89-8 133713-62-9 161686-44-8 165546-16-7
 178032-63-8 402724-66-7 402725-01-3 402725-38-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of **antiviral** nucleoside derivs. as inhibitors of
 subgenomic **hepatitis C virus** RNA
 replication)

IT 3001-45-4P 4753-04-2P 14795-38-1P 25692-02-8P 26287-73-0P
 67912-88-3P 79200-54-7P 87190-77-0P 87413-09-0P, Dess-Martin reagent
 109923-74-2P 402724-61-2P 402724-68-9P 402724-69-0P 402725-17-1P
 402725-18-2P 402725-24-0P 402725-25-1P 402725-27-3P 402725-28-4P
 402725-29-5P 402725-30-8P 402725-31-9P 402725-32-0P 402725-33-1P
 402725-34-2P 402725-35-3P 402725-36-4P 402725-37-5P 402725-39-7P
 402725-40-0P 402725-41-1P 402725-42-2P 402725-43-3P 402725-44-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)

(preparation of **antiviral** nucleoside derivs. as inhibitors of
 subgenomic **hepatitis C virus** RNA
 replication)

IT 2341-22-2P 4298-10-6P 265988-77-0P

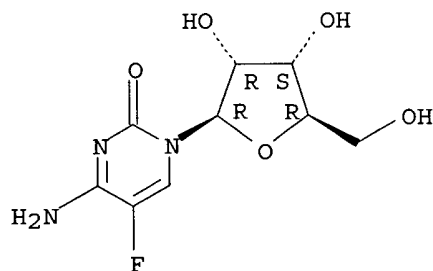
RL: PAC (Pharmacological activity); SPN (Synthetic preparation);
 THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)

(preparation of **antiviral** nucleoside derivs. as inhibitors of
 subgenomic **hepatitis C virus** RNA
 replication)

RN 2341-22-2 HCAPLUS

CN Cytidine, 5-fluoro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

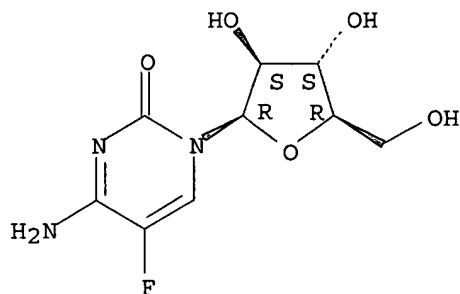
Absolute stereochemistry.



RN 4298-10-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-beta-D-arabinofuranosyl-5-fluoro- (9CI)
 (CA INDEX NAME)

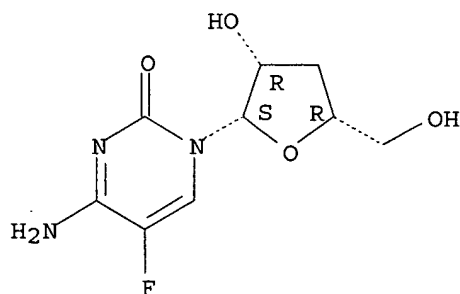
Absolute stereochemistry.



RN 265988-77-0 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(3-deoxy- β -L-threo-pentofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L34 ANSWER 22 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN .

ACCESSION NUMBER: 2001:935354 HCAPLUS

DOCUMENT NUMBER: 136:64094

TITLE: The use of synthetic, non-hormonal 21-aminosteroids, derivatives, metabolites, and precursors thereof in the treatment of **viral** infections

INVENTOR(S): Prendergast, Patrick Thomas

PATENT ASSIGNEE(S): Kotze, Gavin Salomon, S. Afr.

SOURCE: PCT Int. Appl., 47 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001097749	A2	20011227	WO 2001-IB1101	20010622
WO 2001097749	A3	20020523		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,				

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2001074383 A5 20020102 AU 2001-74383 20010622
PRIORITY APPLN. INFO.: IE 2000-511 A 20000623
IE 2001-275 A 20010321
WO 2001-IB1101 W 20010622

AB The invention discloses the use of synthetic, non-hormonal
21-aminosteroids, derivs., metabolites, and precursors thereof in the
treatment of viral infections, particularly **hepatitis** and
retroviral infection by HIV. Synthetic non-hormonal 21-aminosteroids are
disclosed for use in the prophylaxis and therapy of **hepatitis**
viral infections. These compds. can be administered alone or in
combination with conventional **antiviral** agents.

IC ICM A61K

CC 1-5 (Pharmacology)

ST **antiviral** aminosteroid **hepatitis** virus HIV

IT AIDS (disease)

(AIDS-related syndromes; aminosteroids, derivs., metabolites, and
precursors for treatment of **viral** infection, and use with
other agents)

IT Steroids, biological studies

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(amino; aminosteroids, derivs., metabolites, and precursors for
treatment of **viral** infection, and use with other agents)

IT Animal virus

Anti-AIDS agents

Antiviral agents

Border disease virus 1

Bovine diarrhea virus

Cachexia

Classical swine fever virus

Cytomegalovirus

Drug delivery systems

Hepatitis A virus

Hepatitis B virus

Hepatitis C virus

Hepatitis delta virus

Hepatitis virus

Herpesviridae

Human herpesvirus 4

Human immunodeficiency virus

Immunomodulators

Newborn

Retroviridae

(aminosteroids, derivs., metabolites, and precursors for treatment of
viral infection, and use with other agents)

IT Nucleoside analogs

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(aminosteroids, derivs., metabolites, and precursors for treatment of
viral infection, and use with other agents)

IT Antibodies and Immunoglobulins

Carbohydrates, biological studies

Polymers, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(aminosteroids, derivs., metabolites, and precursors for treatment of
viral infection, and use with other agents)

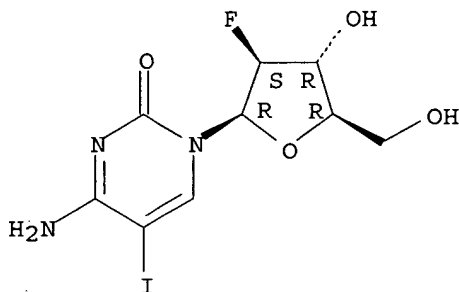
IT Drug delivery systems

- (enteric-coated; aminosteroids, derivs., metabolites, and precursors for treatment of **viral** infection, and use with other agents)
- IT Drug delivery systems
 - (enteric; aminosteroids, derivs., metabolites, and precursors for treatment of **viral** infection, and use with other agents)
- IT Salts, biological studies
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (halogen salts; aminosteroids, derivs., metabolites, and precursors for treatment of **viral** infection, and use with other agents)
- IT Virus
 - (lipid envelope virus; aminosteroids, derivs., metabolites, and precursors for treatment of **viral** infection, and use with other agents)
- IT Drug delivery systems
 - (liposomes; aminosteroids, derivs., metabolites, and precursors for treatment of **viral** infection, and use with other agents)
- IT Drug delivery systems
 - (nasal; aminosteroids, derivs., metabolites, and precursors for treatment of **viral** infection, and use with other agents)
- IT Drug delivery systems
 - (oral; aminosteroids, derivs., metabolites, and precursors for treatment of **viral** infection, and use with other agents)
- IT Drug delivery systems
 - (parenterals; aminosteroids, derivs., metabolites, and precursors for treatment of **viral** infection, and use with other agents)
- IT Drug delivery systems
 - (rectal; aminosteroids, derivs., metabolites, and precursors for treatment of **viral** infection, and use with other agents)
- IT Drug delivery systems
 - (solns., i.v.; aminosteroids, derivs., metabolites, and precursors for treatment of **viral** infection, and use with other agents)
- IT Amines, biological studies
 - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (steroidal; aminosteroids, derivs., metabolites, and precursors for treatment of **viral** infection, and use with other agents)
- IT Drug delivery systems
 - (suppositories; aminosteroids, derivs., metabolites, and precursors for treatment of **viral** infection, and use with other agents)
- IT Drug delivery systems
 - (topical; aminosteroids, derivs., metabolites, and precursors for treatment of **viral** infection, and use with other agents)
- IT Drug delivery systems
 - (unit doses; aminosteroids, derivs., metabolites, and precursors for treatment of **viral** infection, and use with other agents)
- IT Drug delivery systems
 - (vaginal; aminosteroids, derivs., metabolites, and precursors for treatment of **viral** infection, and use with other agents)
- IT Antigens
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (**viral**, antibodies to; aminosteroids, derivs., metabolites, and precursors for treatment of **viral** infection, and use with other agents)
- IT Disease, animal
 - (wasting; aminosteroids, derivs., metabolites, and precursors for treatment of **viral** infection, and use with other agents)
- IT Interferons
 - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

- (α ; aminosteroids, derivs., metabolites, and precursors for treatment of **viral** infection, and use with other agents)
- IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β ; aminosteroids, derivs., metabolites, and precursors for treatment of **viral** infection, and use with other agents)
- IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(γ ; aminosteroids, derivs., metabolites, and precursors for treatment of **viral** infection, and use with other agents)
- IT 54-42-2, Idoxuridine 69-74-9, Cytarabine hydrochloride 70-00-8, Trifluridine 127-07-1, Hydroxyurea 665-66-7, Amantadine hydrochloride 1501-84-4, Rimantadine hydrochloride 1910-68-5, Methisazone 2751-09-9, Triacetyloleandomycin 3056-17-5, d4T 5536-17-4, Vidarabine 7481-89-2, DdC 9004-70-0, HE-2000 10500-82-0, Famotidine hydrochloride 10540-97-3, 11006-77-2, Statolon 15176-29-1, Edoxudine 15185-43-0, DOTC 19885-51-9, Aranotin 25526-93-6, Alovudine 27591-69-1, Tilorone hydrochloride 27762-78-3, Kethoxal 29984-33-6, Vidarabine phosphate 30516-87-1, AZT 35607-20-6, Avridine 36791-04-5, Ribavirin 36983-81-0, Fosfonet sodium 39809-25-1, Penciclovir 56219-57-9, Arildone 59277-89-3, Acyclovir 63198-97-0, Viroxime 63585-09-1, Foscarnet sodium 65277-42-1, Ketoconazole 68693-30-1
69123-90-6, Fiacitabine 69123-98-4, Fialuridine 69655-05-6, DdI 69657-51-8, Acyclovir sodium 71002-10-3 72301-78-1, Zinviroxime 72301-79-2, Enviroxime 73514-87-1, Fosarilate 77181-69-2, Sorivudine 80883-55-2, Enviradene 82410-32-0, Ganciclovir 84408-37-7, Desciclovir 87495-31-6, Disoxaril 104227-87-4, Famciclovir 106362-32-7, Peptide T 106941-25-7, PMEA 107910-75-8, Ganciclovir sodium 110042-95-0, Acemannan 110101-66-1, Tirilazad 110101-66-1D, Tirilazad, metabolites 110101-67-2, Tirilazad mesylate 110143-10-7, Lodenosine 113852-37-2, Cidofovir 124436-59-5, Pirodavis 124832-27-5, Valacyclovir hydrochloride 127759-89-1, Lobucavir 127779-20-8, Saquinavir 129618-40-2, Nevirapine 132210-43-6, Cipamfylline 134678-17-4, 3TC 136470-78-5, Abacavir 136817-59-9, Delavirdine 137487-62-8, Alvircept sudotox 138540-32-6, Ateviridine mesylate 142340-99-6 142632-32-4, Calanolide A 143491-57-0, BW 1592 145514-04-1, DAPD 147127-20-6, Tenofovir 147221-93-0, Delavirdine mesylate 147318-81-8, KNI-272 147362-57-0, Loviride 149845-06-7, Saquinavir mesylate 149950-60-7, Emivirine 150378-17-9, Indinavir 153127-49-2, ALX40-4C 154598-52-4, DMP 266 155148-31-5, AMD 3100 155213-67-5, Ritonavir 157744-31-5 157744-31-5D, metabolites 159519-65-0, Pentafuside 159989-64-7, Nelfinavir 162758-91-0 162758-91-0D, metabolites 163451-80-7, HBY097 170020-61-8, FP-21399 174484-41-4, Tipranavir 177180-81-3 177180-81-3D, metabolites 177180-82-4 177180-82-4D, metabolites 177932-89-7, DMP-450 178979-85-6, AG 1549 185220-03-5, PNU142721 192725-17-0, ABT-378 214287-88-4, DPC 961 216863-66-0, L-756423 251562-00-2, T-1249 383198-55-8, Naragin 383198-56-9, BW 141 383198-57-0, BMS 232630 383198-58-1, PRO 542
RL: **PAC (Pharmacological activity); THU (Therapeutic use);** BIOL (Biological study); USES (Uses)
(aminosteroids, derivs., metabolites, and precursors for treatment of **viral** infection, and use with other agents)
- IT 80-62-6, Methyl methacrylate 2867-47-2, 2-Dimethylaminoethyl methacrylate 9003-63-8, Poly(butyl methacrylate) 9004-38-0, Cellulose acetate phthalate 9050-31-1, Hydroxypropylmethylcellulose phthalate 12619-70-4, Cyclodextrin 12619-70-4D, Cyclodextrin, derivs. 34346-01-5, Poly(lactic acid-glycolic acid)

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aminosteroids, derivs., metabolites, and precursors for treatment of
viral infection, and use with other agents)
IT 9068-38-6, Reverse transcriptase 144114-21-6, Retropepsin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; aminosteroids, derivs., metabolites, and precursors for
treatment of **viral** infection, and use with other agents)
IT 69123-90-6, Fiacitabine
RL: PAC (Pharmacological activity); THU (Therapeutic
use); BIOL (Biological study); USES (Uses)
(aminosteroids, derivs., metabolites, and precursors for treatment of
viral infection, and use with other agents)
RN 69123-90-6 HCAPLUS
CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy-2-fluoro- β -D-arabinofuranosyl)-
5-iodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

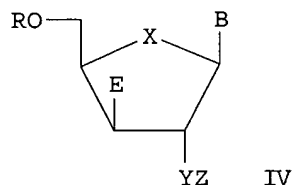
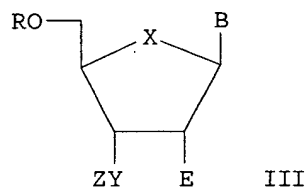
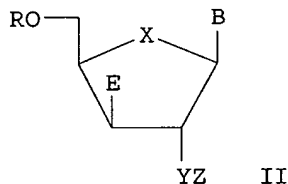
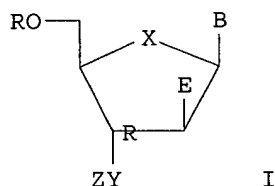


L34 ANSWER 23 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:780927 HCAPLUS
DOCUMENT NUMBER: 135:318659
TITLE: Preparation of 3'-or 2'-hydroxymethyl substituted
nucleoside and nucleotides for treatment of
hepatitis virus infections
INVENTOR(S): Watanabe, Kyoichi A.; Pai, Balakrishna S.
PATENT ASSIGNEE(S): Pharmasset, Ltd., Barbados
SOURCE: PCT Int. Appl., 175 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001079246	A2	20011025	WO 2001-US12050	20010413
WO 2001079246	A3	20020815		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,

BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
CA 2404639 AA 20011025 CA 2001-2404639 20010413
US 2002055483 A1 20020509 US 2001-834596 20010413
US 7094770 B2 20060822
EP 1284741 A2 20030226 EP 2001-932551 20010413
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2003532643 T2 20031105 JP 2001-576844 20010413
BR 2001010023 A 20031230 BR 2001-10023 20010413
PRIORITY APPLN. INFO.: US 2000-197068P P 20000413
US 2000-202663P P 20000508
WO 2001-US12050 W 20010413
OTHER SOURCE(S): MARPAT 135:318659
GI



AB The present invention relates to a composition for and a method of treating **hepatitis B virus (HBV) infection, hepatitis C virus (HCV) infection, hepatitis D virus (HDV) infection** or a proliferative disorder in a patient using an effective amount of a compound selected from the group consisting of nucleoside or nucleotide I-IV mixts. of two or more wherein E is selected from the group consisting of H, OH, OMe, SH, SMe, NH₂, NHMe, N, F, Cl, Br, COH, CO₂-alkyl, OPh, OPhNO, NO, NO₂, SCN, OCN, NCS, NCO, SMe, SMe; X is selected from the group consisting of O, S, NH, CH, CHF, CF; Y is selected from the group consisting of CH, NH, NOH, NMe, NEt, NOME, CHF, CF; Z is selected from the group consisting of H, OH, OMe, SH, SMe, F, Cl, Br, I, NH, NHMe; B is a nucleobase, R is a phosphate derivative. Pharmaceutical compns. comprising these compds. in combination with other HBV, **HCV**, or HDV agents is also disclosed. Thus, 1-[2,3-Dideoxy-2-β-fluoro-3-(N-hydroxy-N-iso-butylamino)-α-D-arabinofuranosyl]-5-fluoro-uracil was prepared and tested in vitro for its **antiviral** activity.

IC ICM C07H019-00
CC 33-9 (Carbohydrates)
Section cross-reference(s): 1, 63
ST nucleoside nucleotide hydroxymethyl prepn **antiviral**

hepatitis

IT **Antiviral agents**

Hepatitis B virus

Hepatitis C virus

Hepatitis delta virus

(preparation of or hydroxymethyl substituted nucleoside and nucleotides for treatment of **hepatitis** virus infections)

IT Nucleosides, preparation

Nucleotides, preparation

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of or hydroxymethyl substituted nucleoside and nucleotides for treatment of **hepatitis** virus infections)

IT 7481-90-5P 132235-71-3P 150968-76-6P 172469-16-8P 172469-24-8P
181045-03-4P 181045-04-5P 195608-72-1P 219841-77-7P 219841-78-8P
219841-79-9P 219841-80-2P 219841-81-3P 367491-84-7P 367491-85-8P
367491-86-9P 367491-87-0P 367491-88-1P 367491-89-2P 367491-90-5P
367491-91-6P 367491-92-7P 367491-93-8P 367491-94-9P 367491-95-0P
367491-96-1P 367491-97-2P **367491-98-3P** 367491-99-4P
367492-00-0P **367492-01-1P** 367492-02-2P 367492-03-3P
367492-04-4P 367492-05-5P 367492-06-6P **367492-07-7P**
367492-08-8P 367492-09-9P 367492-10-2P 367492-11-3P 367492-12-4P
367492-13-5P 367492-14-6P 367492-15-7P 367492-16-8P 367492-17-9P
367493-44-5P 367493-45-6P

RL: **BAC** (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); **THU** (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of or hydroxymethyl substituted nucleoside and nucleotides for treatment of **hepatitis** virus infections)

IT 219841-70-0P 219841-71-1P 219841-73-3P 219841-74-4P 367491-77-8P
367491-78-9P 367491-79-0P 367491-80-3P 367491-81-4P 367491-82-5P
367491-83-6P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of or hydroxymethyl substituted nucleoside and nucleotides for treatment of **hepatitis** virus infections)

IT 4229-44-1, N-Methylhydroxylamine Hydrochloride 154540-17-7

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of or hydroxymethyl substituted nucleoside and nucleotides for treatment of **hepatitis** virus infections)

IT **367491-98-3P 367492-01-1P 367492-07-7P**

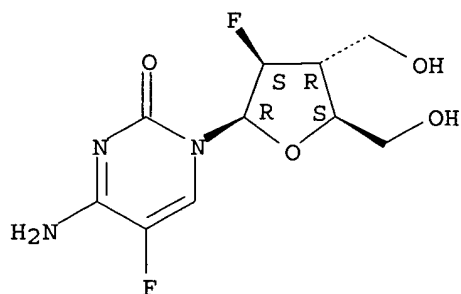
RL: **BAC** (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); **THU** (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of or hydroxymethyl substituted nucleoside and nucleotides for treatment of **hepatitis** virus infections)

RN 367491-98-3 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-[2,3-dideoxy-2-fluoro-3-(hydroxymethyl)- β -D-arabinofuranosyl]-5-fluoro- (9CI) (CA INDEX NAME)

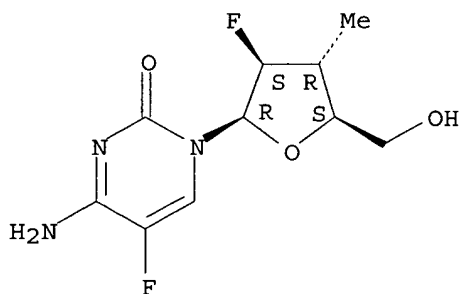
Absolute stereochemistry.



RN 367492-01-1 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2,3-dideoxy-2-fluoro-3-methyl- β -D-arabinofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

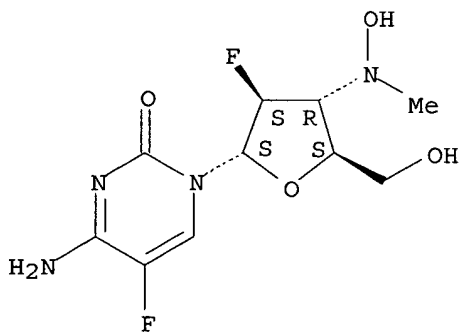
Absolute stereochemistry.



RN 367492-07-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-[2,3-dideoxy-2-fluoro-3-(hydroxymethylamino)- α -D-arabinofuranosyl]-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L34 ANSWER 24 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:674936 HCAPLUS

DOCUMENT NUMBER: 136:47974

TITLE: Anti-HBV specific β -L-2'-deoxynucleosides

AUTHOR(S): Bryant, Martin L.; Bridges, Edward G.; Placidi, Laurent; Faraj, Abdesslem; Loi, Anna-Giulia; Pierra,

Claire; Dukhan, David; Gosselin, Gilles; Imbach, Jean-Louis; Hernandez, Brenda; Juodawlkis, Amy; Tennant, Bud; Korba, Brent; Cote, Paul; Cretton-Scott, Erika; Schinazi, Raymond F.; Sommadossi, Jean-Pierre

CORPORATE SOURCE: Novirio Pharmaceuticals, Inc., Cambridge, MA, 02476, USA

SOURCE: Nucleosides, Nucleotides & Nucleic Acids (2001), 20(4-7), 597-607
CODEN: NNNAFY; ISSN: 1525-7770

PUBLISHER: Marcel Dekker, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A unique series of simple unnatural L-nucleosides that specifically inhibit **hepatitis** B virus (HBV) replication has been discovered. These mols. have in common a hydroxyl group in the 3'-position (3'-OH) of the β -L-2'-deoxyribose sugar that confers **antiviral** activity specifically against hepadnaviruses. Replacement of the 3'-OH broadens activity to other viruses. Substitution in the base decreases **antiviral** potency and selectivity. Human DNA polymerases and mitochondrial function are not effected. Plasma viremia is reduced up to 8 logs in a woodchuck model of chronic HBV infection. These investigational drugs, used alone or in combination, are expected to offer new therapeutic options for patients with chronic HBV infection.

CC 1-3 (Pharmacology)

ST deoxynucleoside **antiviral** hepadnaviridae **hepatitis** B virus structure activity

IT **Antiviral** agents
Hepadnaviridae
 Hepatitis B virus
 Human adenovirus 1
 Human herpesvirus 4
 Human immunodeficiency virus 1
 Human immunodeficiency virus 2
 Human parainfluenza virus 3
 Influenza A virus
 Influenza B virus
 Measles virus
 Mitochondria
 Woodchuck **hepatitis** virus
 (anti-HBV specific β -L-2'-deoxynucleosides structure-activity relationships)

IT **Viral** DNA
RL: BSU (Biological study, unclassified); BIOL (Biological study) (anti-HBV specific β -L-2'-deoxynucleosides structure-activity relationships)

IT Structure-activity relationship
 (**antiviral**; anti-HBV specific β -L-2'-deoxynucleosides structure-activity relationships)

IT 3424-98-4 14365-45-8 40093-94-5 61246-68-2 121154-51-6
127501-59-1 128075-91-2 132979-39-6 134678-17-4 135212-56-5
135212-57-6 143491-57-0 144490-02-8 **147058-39-7**
160963-01-9 **160963-15-5** 177365-14-9 181785-84-2
182929-00-6 182929-01-7 186648-57-7 201295-39-8 216571-37-8
244097-84-5 **265988-73-6** **374107-79-6**
381719-94-4 **381719-95-5** 381719-96-6
RL: **PAC** (**Pharmacological activity**); **THU** (**Therapeutic use**); BIOL (Biological study); USES (Uses)
 (anti-HBV specific β -L-2'-deoxynucleosides structure-activity relationships)

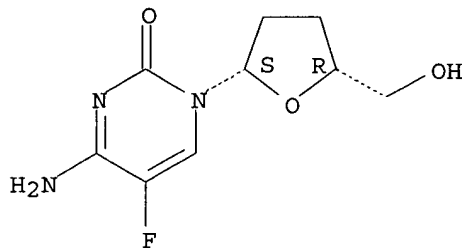
IT 147058-39-7 160963-15-5 265988-73-6
374107-79-6 381719-94-4 381719-95-5

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-HBV specific β -L-2'-deoxynucleosides structure-activity relationships)

RN 147058-39-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

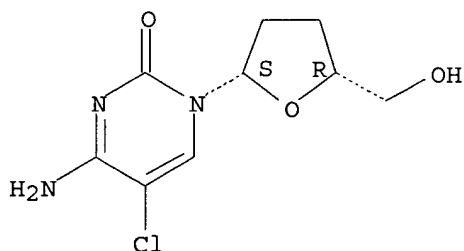
Absolute stereochemistry. Rotation (-).



RN 160963-15-5 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-chloro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

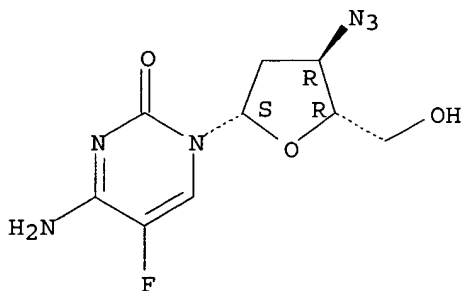
Absolute stereochemistry. Rotation (-).



RN 265988-73-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(3-azido-2,3-dideoxy- β -L-erythro-pentofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

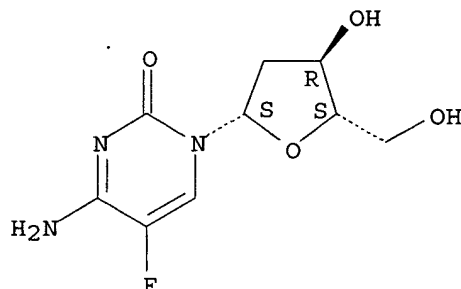
Absolute stereochemistry. Rotation (-).



RN 374107-79-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy- β -L-erythro-pentofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

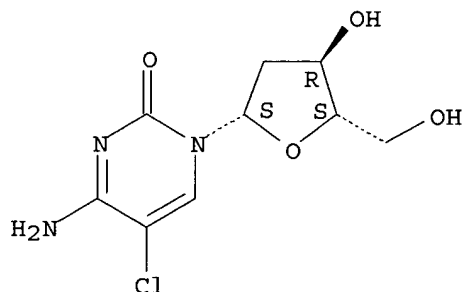
Absolute stereochemistry. Rotation (-).



RN 381719-94-4 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-chloro-1-(2-deoxy- β -L-erythro-pentofuranosyl)- (9CI) (CA INDEX NAME)

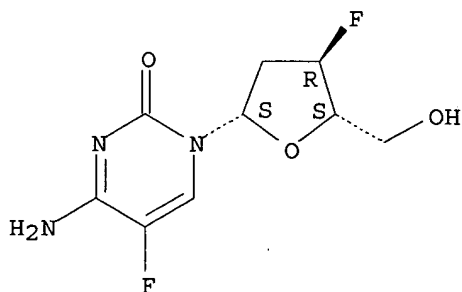
Absolute stereochemistry.



RN 381719-95-5 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2,3-dideoxy-3-fluoro- β -L-erythro-pentofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

38

THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 25 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:617821 HCAPLUS
DOCUMENT NUMBER: 135:175348
TITLE: Use of N-substituted-1,5-dideoxy-1,5-imino-D-glucitol
compounds for treating **hepatitis** virus
infections
INVENTOR(S): Mueller, Richard A.; Bryant, Martin L.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2001060366	A1	20010823	WO 2001-US4512	20010213
W:			AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM	
RW:			GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG	
AU 2001036938	A5	20010827	AU 2001-36938	20010213
EP 1261339	A1	20021204	EP 2001-909153	20010213
R:			AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR	
JP 2003522791	T2	20030729	JP 2001-559463	20010213
US 2005119310	A1	20050602	US 2002-203769	20010213
PRIORITY APPLN. INFO.:			US 2000-182362P	P 20000214
			WO 2001-US4512	W 20010213
AB	Provided are methods and compns. for treating hepatitis virus infections in mammals, especially humans. The methods comprise (1) administering N-substituted-1,5-dideoxy-1,5-imino-D-glucitol compds. alone or in combination with nucleoside antiviral agents, nucleotide antiviral agents, mixts. thereof, or immunomodulating/immunostimulating agents, or (2) administering N-substituted-1,5-dideoxy-1,5-imino-D-glucitol compds. alone or in combination with nucleoside antiviral agents, nucleotide antiviral agents, or mixts. thereof, and immunomodulating/immuno stimulating agents.			
IC	ICM A61K031-445			
	ICS A61P031-14			
CC	1-5 (Pharmacology)			
ST	hepatitis virus iminoglucitol deriv nucleoside nucleotide; immunomodulator antiviral hepatitis virus iminoglucitol deriv			
IT	Hepatitis (B; treatment of hepatitis B and C virus infections with dideoxyiminoglucitols and antiviral nucleosides and nucleotides)			
IT	Hepatitis (C; treatment of hepatitis B and C virus infections with dideoxyiminoglucitols and antiviral nucleosides and nucleotides)			

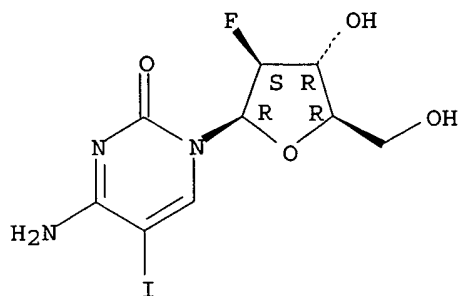
IT **Antiviral agents**
 Hepatitis B virus
 Hepatitis C virus
Immunomodulators
Immunostimulants
 (treatment of **hepatitis B** and C virus infections with
 dideoxyiminoglucitols and **antiviral** nucleosides and
 nucleotides)

IT 3056-17-5, Stavudine 5536-17-4, Ara-A 7481-89-2, Dideoxycytidine
25526-93-6 29984-33-6, Ara-AMP 30516-87-1, 3'-Azido-3'-deoxythymidine
36791-04-5, 1- β -D-Ribofuranosyl-1,2,4-triazole-3-carboxamide
39809-25-1, Penciclovir 59277-89-3, Acyclovir 66341-18-2, Acyclovir
triphosphate **69123-90-6**, FIAC 69123-98-4, FIAU 69256-17-3,
FMAU 69655-05-6, Dideoxyinosine 72458-45-8 72458-46-9 73243-67-1
77222-61-8 79206-10-3 79206-12-5 79206-14-7 79206-20-5
79206-22-7 **79570-63-1** 81117-35-3 81117-36-4 81117-38-6
82410-32-0, Ganciclovir 85326-06-3 87190-81-6 104227-87-4,
Famciclovir 106941-25-7, PMEA 111687-37-7, D-Carbocyclic-2'-
deoxyguanosine 115183-38-5 115249-95-1 121154-51-6 128985-11-5
131167-83-4 134678-17-4, 3TC 134680-32-3 137530-41-7 143491-54-7,
FTC 143491-57-0 143616-58-4 **147058-39-7** 160632-03-1
160632-05-3 162398-48-3 162398-56-3 211987-28-9 211987-29-0
211987-30-3 211987-31-4 211987-32-5 211987-33-6 211987-34-7
211987-35-8 211987-36-9 211987-37-0 211987-38-1 211987-39-2
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211987-50-7 211987-51-8 211987-52-9 211987-53-0 211987-54-1
211987-55-2 211987-56-3 211987-57-4 211987-58-5 211987-59-6
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238075-09-7 238075-10-0 238075-11-1 238075-12-2 238075-13-3
238075-14-4 238075-15-5 238075-16-6 238075-17-7 238075-18-8
238075-19-9 238075-20-2 238075-21-3 238075-22-4
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); USES (Uses)
 (treatment of **hepatitis B** and C virus infections with
 dideoxyiminoglucitols and **antiviral** nucleosides and
 nucleotides)

IT **69123-90-6**, FIAC **79570-63-1** **147058-39-7**
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); USES (Uses)
 (treatment of **hepatitis B** and C virus infections with
 dideoxyiminoglucitols and **antiviral** nucleosides and
 nucleotides)

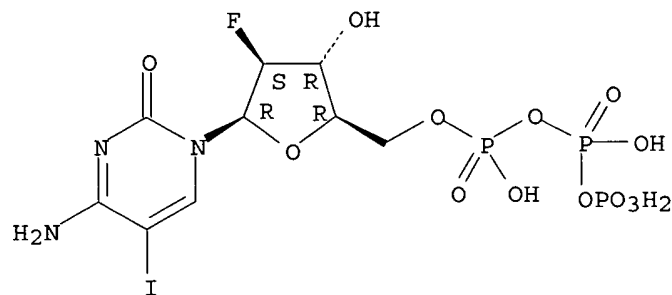
RN 69123-90-6 HCAPLUS
CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy-2-fluoro- β -D-arabinofuranosyl)-
5-iodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



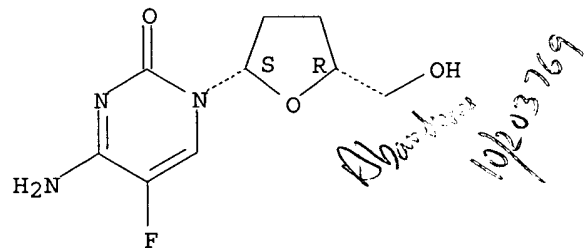
RN 79570-63-1 HCAPLUS
CN 2(1H)-Pyrimidinone, 4-amino-1-[2-deoxy-2-fluoro-5-O-[hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]]-β-D-arabinofuranosyl]-5-iodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 147058-39-7 HCAPLUS
CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 26 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:617773 HCAPLUS
DOCUMENT NUMBER: 135:175346
TITLE: Method for the treatment or prevention of flavivirus infections using nucleoside analogues
INVENTOR(S): Ismaili, Hicham Moulay Alaoui; Cheng, Yun-Xing;

Lavallee, Jean-Francois; Siddiqui, Arshad; Storer, Richard
PATENT ASSIGNEE(S): Biochem Pharma Inc., Can.
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060315	A2	20010823	WO 2001-CA197	20010219
WO 2001060315	A3	20030116		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2400274	AA	20010823	CA 2001-2400274	20010219
AU 2001035278	A5	20010827	AU 2001-35278	20010219
EP 1296690	A2	20030402	EP 2001-907276	20010219
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2003523978	T2	20030812	JP 2001-559414	20010219
NZ 521210	A	20041126	NZ 2001-521210	20010219
US 2002019363	A1	20020214	US 2001-785235	20010220
US 6784161	B2	20040831		
ZA 2002006506	A	20031114	ZA 2002-6506	20020814
NO 2002003884	A	20021017	NO 2002-3884	20020816
US 2004248844	A1	20041209	US 2004-887292	20040709
PRIORITY APPLN. INFO.:			US 2000-183349P	P 20000218
			WO 2001-CA197	W 20010219
			US 2001-785235	A1 20010220

OTHER SOURCE(S): MARPAT 135:175346

AB The present invention relates to a method for the treatment or prevention of Flavivirus infections using nucleoside analogs in a host comprising administering a therapeutically effective amount of the nucleoside analog or a pharmaceutically acceptable salt thereof.

IC ICM A61K

CC 1-5 (Pharmacology)

Section cross-reference(s): 33

ST flavivirus infection treatment prevention nucleoside analog;

hepatitis C virus infection nucleoside analog

IT **Antiviral** agents

Drug delivery systems

Drug interactions

Flavivirus

Hepatitis C virus

Silybum marianum

(method for treatment or prevention of flavivirus infections using nucleoside analogs and their combination with other agents in relation to **hepatitis C virus** RNA-dependent RNA polymerase (NS5B protein))

IT Interferons

Interleukin 12

Nucleoside analogs

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(method for treatment or prevention of flavivirus infections using nucleoside analogs and their combination with other agents in relation to **hepatitis C virus** RNA-dependent RNA polymerase (NS5B protein))

IT Interferons

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(α -2a; method for treatment or prevention of flavivirus infections using nucleoside analogs and their combination with other agents in relation to **hepatitis C virus** RNA-dependent RNA polymerase (NS5B protein))

IT Interferons

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(α -2b; method for treatment or prevention of flavivirus infections using nucleoside analogs and their combination with other agents in relation to **hepatitis C virus** RNA-dependent RNA polymerase (NS5B protein))

IT 355805-74-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(method for treatment or prevention of flavivirus infections using nucleoside analogs and their combination with other agents in relation to **hepatitis C virus** RNA-dependent RNA polymerase (NS5B protein))

IT 128-13-2, Ursodeoxycholic acid 611-60-9, 3'-Deoxythymidine-5'-triphosphate 768-94-5, Amantadine 1405-86-3, Glycyrrhizin 2004-07-1 3416-05-5, 3'-Deoxythymidine 3530-56-1 3608-58-0, 3'-Deoxyguanosine 7057-27-4, 3'-Deoxyuridine 7057-33-2, 3'-Deoxycytidine 7057-38-7 13392-28-4, Rimantadine 18829-83-9, 5-Fluoro-3'-deoxyuridine **18829-84-0** 27462-39-1 36791-04-5, Ribavirin 55968-37-1, 3'-Deoxyguanosine-5'-triphosphate 69199-40-2, 3'-Deoxyuridine-5'-triphosphate 69383-05-7 70580-87-9 85395-67-1 85708-20-9 99909-03-2 **99909-04-3** 123402-20-0 123402-21-1 123402-25-5 123402-27-7 **130860-14-9** 134660-26-7 141320-63-0 355805-44-6 355805-45-7 355805-46-8 **355805-47-9** **355805-48-0** **355805-49-1** 355805-50-4 355805-51-5 355805-52-6 355805-55-9 355805-57-1 355805-59-3 355805-60-6 355805-61-7 355805-62-8 355805-63-9 355805-64-0 355805-65-1 355805-66-2 355805-67-3 355805-68-4 355805-69-5 355805-70-8 355805-71-9 355805-72-0 355805-73-1

RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(method for treatment or prevention of flavivirus infections using nucleoside analogs and their combination with other agents in relation to **hepatitis C virus** RNA-dependent RNA polymerase (NS5B protein))

IT 9026-28-2, RNA-dependent RNA polymerase

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(method for treatment or prevention of flavivirus infections using nucleoside analogs and their combination with other agents in relation to **hepatitis C virus** RNA-dependent RNA polymerase (NS5B protein))

IT 50859-18-2, Tributylammonium pyrophosphate 355805-75-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(method for treatment or prevention of flavivirus infections using nucleoside analogs and their combination with other agents in relation to **hepatitis C virus** RNA-dependent RNA polymerase (NS5B protein))

IT 18829-84-0 99909-04-3 130860-14-9
355805-47-9 355805-48-0 355805-49-1

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); THU (Therapeutic use); BIOL

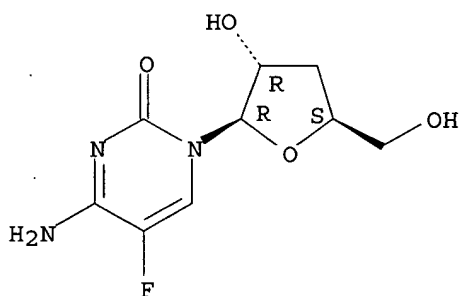
(Biological study); USES (Uses)

(method for treatment or prevention of flavivirus infections using nucleoside analogs and their combination with other agents in relation to **hepatitis C virus** RNA-dependent RNA polymerase (NS5B protein))

RN 18829-84-0 HCAPLUS

CN Cytidine, 3'-deoxy-5-fluoro- (8CI, 9CI) (CA INDEX NAME)

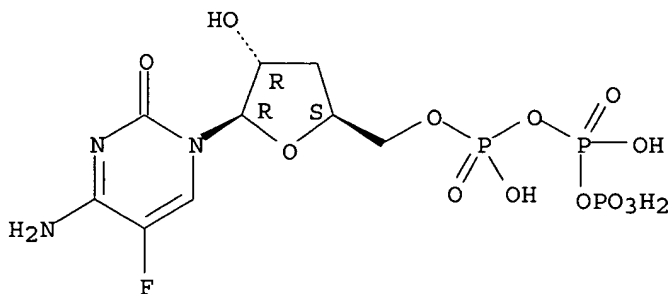
Absolute stereochemistry.



RN 99909-04-3 HCAPLUS

CN Cytidine 5'-(tetrahydrogen triphosphate), 3'-deoxy-5-fluoro- (9CI) (CA INDEX NAME)

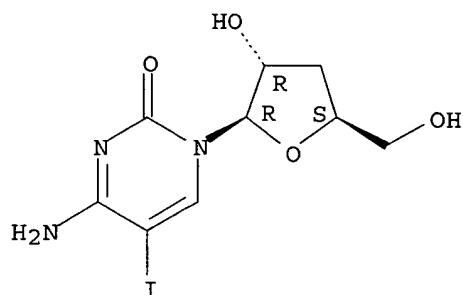
Absolute stereochemistry.



RN 130860-14-9 HCAPLUS

CN Cytidine, 3'-deoxy-5-iodo- (9CI) (CA INDEX NAME)

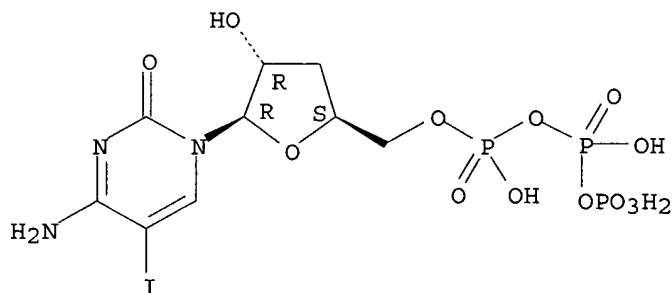
Absolute stereochemistry.



RN 355805-47-9 HCAPLUS

CN Cytidine 5'-(tetrahydrogen triphosphate), 3'-deoxy-5-iodo- (9CI) (CA INDEX NAME)

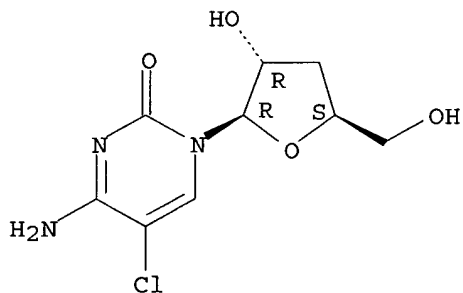
Absolute stereochemistry.



RN 355805-48-0 HCAPLUS

CN Cytidine, 5-chloro-3'-deoxy- (9CI) (CA INDEX NAME)

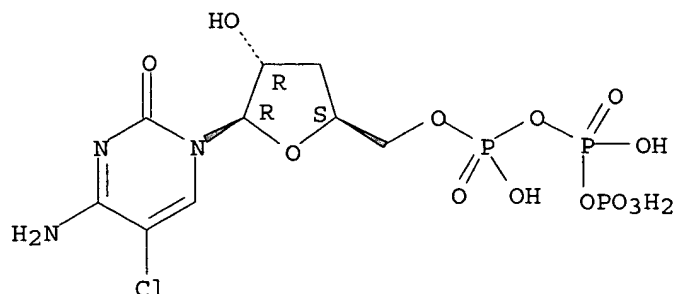
Absolute stereochemistry.



RN 355805-49-1 HCAPLUS

CN Cytidine 5'-(tetrahydrogen triphosphate), 5-chloro-3'-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L34 ANSWER 27 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:131768 HCAPLUS

DOCUMENT NUMBER: 135:13822

TITLE: The polymerase L528M mutation cooperates with nucleotide binding-site mutations, increasing **hepatitis** B virus replication and drug resistance

AUTHOR(S): Ono, Suzane Kioko; Kato, Naoya; Shiratori, Yasushi; Kato, Jun; Goto, Tadashi; Schinazi, Raymond F.; Carrilho, Flair Jose; Omata, Masao

CORPORATE SOURCE: Department of Gastroenterology, Faculty of Medicine, University of Tokyo, Tokyo, 113-8655, Japan

SOURCE: Journal of Clinical Investigation (2001), 107(4), 449-455

CODEN: JCINAO; ISSN: 0021-9738

PUBLISHER: American Society for Clinical Investigation

DOCUMENT TYPE: Journal

LANGUAGE: English

AB After receiving lamivudine for 3 yr to treat chronic **hepatitis** B (HBV), 67-75% of patients develop B-domain L528M, C-domain M552I, or M552V mutations in the HBV polymerase that render HBV drug-resistant. The aim of this study was to evaluate the influence of these mutations on viral replication and resistance to **antiviral** agents. The authors investigated the replication fitness and susceptibility of the wild-type and five mutant HBVs (L528M, M552I, M552V, L528M/M552I, and L528M/M552V) to 11 compds. [lamivudine, adefovir, entecavir (BMS-200475) (+)-BCH-189 (+)-FTC (racivir) (-)-FTC (emtricitabine) (+)-FTC, L-D4FC, L-FMAU (clevudine), D-DAPD, and (-)-carbovir] by transfecting HBV DNA into hepatoma cells and monitoring viral products by Southern blotting. The replication competency of the single C-domain mutants M552I and M552V was markedly decreased compared with that of wild-type HBV. However, addition of the B-domain mutation L528M restored replication competence. Only adefovir and entecavir were effective against all five HBV mutants, and higher doses of these compds. were necessary to inhibit the double mutants compared with the single mutants. The B-domain mutation (L528M) of HBV polymerase not only restores the replication competence of C-domain mutants, but also increases resistance to nucleoside analogs.

CC 1-2 (Pharmacology)

ST **hepatitis** B virus drug resistance polymerase mutation

IT Drug resistance

(**antiviral**; polymerase L528M mutation cooperates with nucleotide binding-site mutations, increasing **hepatitis** B virus replication and drug resistance)

IT **Hepatitis** B virus
Mutation

(polymerase L528M mutation cooperates with nucleotide binding-site mutations, increasing **hepatitis** B virus replication and drug resistance)

IT **Antiviral agents**

(resistance to; polymerase L528M mutation cooperates with nucleotide binding-site mutations, increasing **hepatitis** B virus replication and drug resistance)

IT 106941-25-7, Adefovir 120443-30-3, (-)-Carbovir 134678-17-4, Lamivudine 134680-32-3, (+)-BCH-189 137530-41-7, (+)-FTC 142217-69-4, Entecavir 143491-54-7, Racivir 143491-57-0, Emtricitabine 145514-04-1 **147058-39-7** 163252-36-6, Clevudine

RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(polymerase L528M mutation cooperates with nucleotide binding-site mutations, increasing **hepatitis** B virus replication and drug resistance)

IT 9068-38-6, RNA-dependent DNA polymerase

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(polymerase L528M mutation cooperates with nucleotide binding-site mutations, increasing **hepatitis** B virus replication and drug resistance)

IT **147058-39-7**

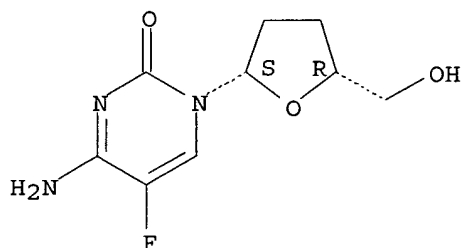
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(polymerase L528M mutation cooperates with nucleotide binding-site mutations, increasing **hepatitis** B virus replication and drug resistance)

RN 147058-39-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 28 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:100967 HCAPLUS

DOCUMENT NUMBER: 134:141721

TITLE: N-Substituted glucamine compounds for treating **hepatitis** virus infections

INVENTOR(S): Mueller, Richard A.; Bryant, Martin L.; Partis, Richard A.

PATENT ASSIGNEE(S): G.D. Searle and Co., USA

SOURCE: PCT Int. Appl., 148 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001008672	A2	20010208	WO 2000-US3816	20000214
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2362785	AA	20010208	CA 2000-2362785	20000214
EP 1173161	A2	20020123	EP 2000-917640	20000214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6515028	B1	20030204	US 2000-503865	20000214
JP 2003505501	T2	20030212	JP 2001-513402	20000214
US 2003195229	A1	20031016	US 2002-322045	20021217
US 6747149	B2	20040608		

PRIORITY APPLN. INFO.:

US 1999-119836P	P	19990212
US 1999-119858P	P	19990212
US 2000-503865	A1	20000214
WO 2000-US3816	W	20000214

OTHER SOURCE(S): MARPAT 134:141721

AB N-Substituted glucamine compds. (Markush included) are effective in treatment of **hepatitis** infections, including **hepatitis** B and **hepatitis** C. In treating **hepatitis** infections, the compds. of the invention may be used alone or in combination with another **antiviral** agent selected from nucleosides, nucleotides, immunomodulators, immunostimulants, or various combinations of such other agents. Preparation of e.g. 1,5-(butylimino)-1,5-dideoxy-D-glucitol tetraacetate is described.

IC ICM A61K031-00

CC 1-5 (Pharmacology)

Section cross-reference(s): 63

ST glucamine deriv prepn **antiviral hepatitis** virus;
 nucleoside glucamine deriv combination **antiviral hepatitis** virus; nucleotide glucamine deriv combination **antiviral hepatitis** virus; immunomodulator glucamine deriv combination **antiviral hepatitis** virus;
 immunostimulant glucamine deriv combination **antiviral hepatitis** virus

IT **Antiviral** agents

Drug delivery systems

Drug interactions

Hepatitis B virus**Hepatitis** C virus**Hepatitis** virus

Immunomodulators

Immunostimulants

Simulation and Modeling, biological

(N-substituted glucamine compds. for treating **hepatitis** virus

infections, and use with other agents)

IT Nucleosides, biological studies
Nucleotides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(N-substituted glucamine compds. for treating **hepatitis** virus infections, and use with other agents)

IT 131262-77-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(N-substituted glucamine compds. for treating **hepatitis** virus infections, and use with other agents)

IT 488-43-7D, Glucamine, derivs. 3056-17-5, Stavudine 5536-17-4, Ara-A 7481-89-2, Dideoxycytidine 25526-93-6 29984-33-6, Ara-AMP 30516-87-1, AZT 36791-04-5 39809-25-1, Penciclovir 59277-89-3, Acyclovir 66341-18-2 **69123-90-6**, FIAC 69123-98-4, FIAU 69256-17-3, FMAU 69655-05-6, Dideoxyinosine 73243-67-1 77222-61-8 **79570-63-1** 80955-98-2 81117-35-3 82410-32-0 85326-06-3 87190-81-6 91840-92-5 100018-53-9 104227-87-4, Famciclovir 106941-25-7, PMEA 115249-95-1 128985-16-0 131167-83-4 131262-82-3 131262-91-4 131262-93-6 134678-17-4 137530-41-7 143491-54-7, FTC 143616-58-4 143698-32-2 143698-33-3 145417-33-0 **147058-39-7** 196406-67-4 288301-59-7 288301-60-0 288301-61-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(N-substituted glucamine compds. for treating **hepatitis** virus infections, and use with other agents)

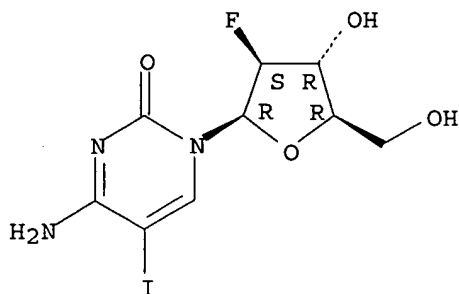
IT 72599-27-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction; N-substituted glucamine compds. for treating **hepatitis** virus infections, and use with other agents)

IT 108-24-7, Acetic anhydride 123-72-8, Butyraldehyde 19130-96-2, 1,5-Dideoxy-1,5-imino-D-glucitol
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; N-substituted glucamine compds. for treating **hepatitis** virus infections, and use with other agents)

IT **69123-90-6**, FIAC **79570-63-1** **147058-39-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(N-substituted glucamine compds. for treating **hepatitis** virus infections, and use with other agents)

RN 69123-90-6 HCAPLUS
CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy-2-fluoro- β -D-arabinofuranosyl)-5-iodo- (9CI) (CA INDEX NAME)

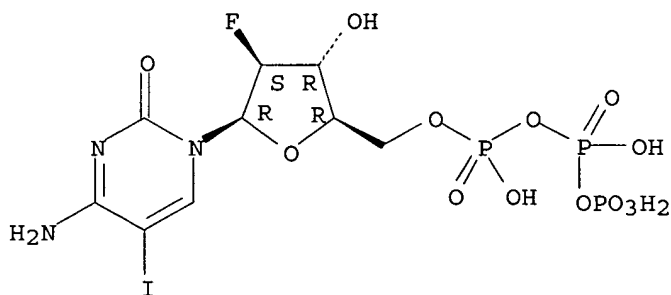
Absolute stereochemistry.



RN 79570-63-1 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-[2-deoxy-2-fluoro-5-O-[hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-β-D-arabinofuranosyl]-5-iodo- (9CI) (CA INDEX NAME)

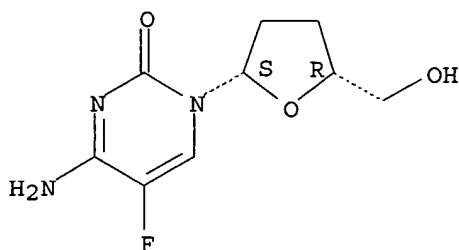
Absolute stereochemistry.



RN 147058-39-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L34 ANSWER 29 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:15521 HCAPLUS

DOCUMENT NUMBER: 134:216812

TITLE: **Antiviral L-nucleosides specific for hepatitis B virus infection**

AUTHOR(S): Bryant, Martin L.; Bridges, Edward G.; Placidi, Laurent; Faraj, Abdesslem; Loi, Anna-Giulia; Pierra, Claire; Dukhan, David; Gosselin, Gilles; Imbach,

Jean-Louis; Hernandez, Brenda; Juodawlkis, Amy;
Tennant, Bud; Korba, Brent; Cote, Paul; Marion, Pat;
Cretton-Scott, Erika; Schinazi, Raymond F.;
Sommadosi, Jean-Pierre

CORPORATE SOURCE: Novirio Pharmaceuticals, Inc., Cambridge, MA, 02140,
USA

SOURCE: Antimicrobial Agents and Chemotherapy (2001), 45(1),
229-235
CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A unique series of simple "unnatural" nucleosides has been discovered to
inhibit **hepatitis** B virus (HBV) replication. Through
structure-activity anal. it was found that the 3'-OH group of the
 β -L-2'-deoxyribose of the β -L-2'-deoxynucleoside confers
specific antihepadnavirus activity. The unsubstituted nucleosides
 β -L-2'-deoxycytidine, β -L-thymidine, and β -L-2'-
deoxyadenosine had the most potent, selective, and specific
antiviral activity against HBV replication. Human DNA polymerases
(α , β , and γ) and mitochondrial function were not
affected. In the woodchuck model of chronic HBV infection, viral load was
reduced by as much as 108 genome equivalent/mL of serum and there was no
drug-related toxicity. In addition, the decline in woodchuck
hepatitis virus surface antigen paralleled the decrease in viral
load. These investigational drugs, used alone or in combination, are
expected to offer new therapeutic options for patients with chronic HBV
infection.

CC 1-3 (Pharmacology)

ST **antiviral** nucleoside analog structure **hepatitis** B
virus

IT **Antiviral** agents
Hepatitis B virus
Mitochondria
(**antiviral** L-nucleosides specific for **hepatitis** B
virus infection)

IT Nucleoside analogs
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or
effector, except adverse); BSU (Biological study, unclassified); PRP
(Properties); BIOL (Biological study)
(**antiviral** L-nucleosides specific for **hepatitis** B
virus infection)

IT Structure-activity relationship
(**antiviral**; **antiviral** L-nucleosides specific for
hepatitis B virus infection)

IT 50-89-5, Thymidine, biological studies 951-77-9 958-09-8 3056-17-5
3416-05-5 4097-22-7 4291-63-8 7057-48-9 7403-25-0 7481-88-1
7481-89-2 10356-76-0 16053-52-4 25526-93-6 26315-32-2D,
terbutyl-S-acylthioethyl derivs. 30516-87-1 32387-56-7
51246-79-8 52450-18-7 66323-44-2 87190-80-5 87418-35-7
107036-62-4 124743-31-3 134379-77-4
134379-78-5 134678-17-4, Lamivudine 143491-54-7, FTC
329722-17-0
RL: ADV (Adverse effect, including toxicity); BAC (Biological
activity or effector, except adverse); BSU (Biological study,
unclassified); PRP (Properties); BIOL (Biological study)
(**antiviral** L-nucleosides specific for **hepatitis** B
virus infection)

IT 9012-90-2, DNA polymerase

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(α , β , and γ ; **antiviral** L-nucleosides specific for **hepatitis B** virus infection)

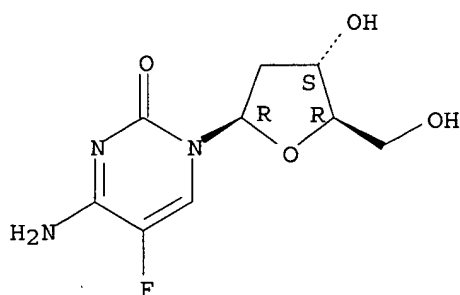
IT 10356-76-0 32387-56-7 87190-80-5
107036-62-4 124743-31-3 134379-78-5

RL: ADV (Adverse effect, including toxicity); **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**antiviral** L-nucleosides specific for **hepatitis B** virus infection)

RN 10356-76-0 HCAPLUS

CN Cytidine, 2'-deoxy-5-fluoro- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

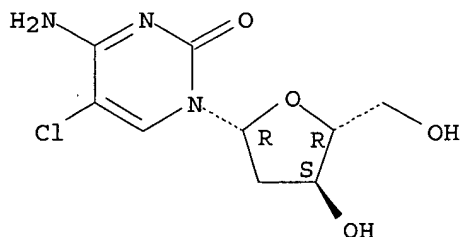
Absolute stereochemistry.



RN 32387-56-7 HCAPLUS

CN Cytidine, 5-chloro-2'-deoxy- (6CI, 8CI, 9CI) (CA INDEX NAME)

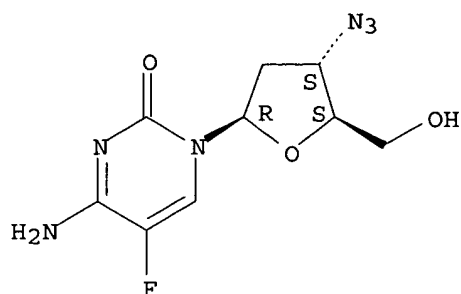
Absolute stereochemistry.



RN 87190-80-5 HCAPLUS

CN Cytidine, 3'-azido-2',3'-dideoxy-5-fluoro- (9CI) (CA INDEX NAME)

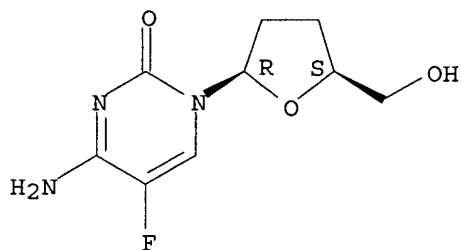
Absolute stereochemistry.



RN 107036-62-4 HCAPLUS

CN Cytidine, 2',3'-dideoxy-5-fluoro- (9CI) (CA INDEX NAME)

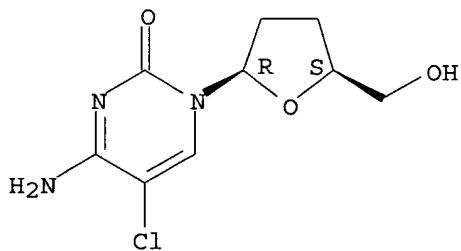
Absolute stereochemistry.



RN 124743-31-3 HCAPLUS

CN Cytidine, 5-chloro-2',3'-dideoxy- (9CI) (CA INDEX NAME)

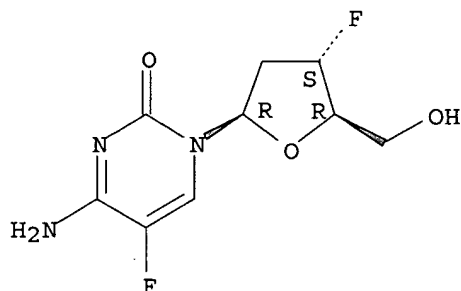
Absolute stereochemistry. Rotation (+).



RN 134379-78-5 HCAPLUS

CN Cytidine, 2',3'-dideoxy-3',5-difluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 30 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:573657 HCAPLUS
DOCUMENT NUMBER: 133:172150
TITLE: Use of substituted-1,5-dideoxy-1,5-imino-D-glucitol compounds for treating hepatitis virus infections
INVENTOR(S): Mueller, Richard A.; Bryant, Martin L.; Partis, Richard A.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 170 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000047198	A2	20000817	WO 2000-US3768	20000214
WO 2000047198	A3	20010215		
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2362914	AA	20000817	CA 2000-2362914	20000214
EP 1165080	A2	20020102	EP 2000-914585	20000214
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
JP 2002536407	T2	20021029	JP 2000-598151	20000214
US 6545021	B1	20030408	US 2000-503945	20000214
EP 1658846	A1	20060524	EP 2005-27240	20000214
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			
US 2003220299	A1	20031127	US 2003-341717	20030114
PRIORITY APPLN. INFO.:			US 1999-119722P	P 19990212
			US 1999-119856P	P 19990212
			EP 2000-914585	A3 20000214
			US 2000-503945	A1 20000214
			WO 2000-US3768	W 20000214

OTHER SOURCE(S): MARPAT 133:172150

- AB N-Substituted-1,5-dideoxy-1,5-imino-D-glucitol compds. are effective in treatment of **hepatitis** infections, including **hepatitis** B and **hepatitis** C. In treating **hepatitis** infections, the tittle compds. may be used alone, or in combination with another **antiviral** agent selected from among nucleosides, nucleotides, immunomodulators, immunostimulants or various combinations of such other agents.
- IC ICM A61K031-00
- CC 1-5 (Pharmacology)
Section cross-reference(s): 33
- ST dideoxyiminoglucitol compd **hepatitis** virus infection treatment
- IT Nucleotides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(analog, **antiviral** agents; use of substituted dideoxyimino-D-glucitol compds. for treating **hepatitis** virus infections and combination with other **antiviral** agents or immunostimulants)
- IT Nucleoside analogs
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**antiviral** agents; use of substituted dideoxyimino-D-glucitol compds. for treating **hepatitis** virus infections and combination with other **antiviral** agents or immunostimulants)
- IT **Antiviral** agents
Drug delivery systems
Drug interactions
Hepatitis B virus
Hepatitis C virus
Hepatitis virus
Immunomodulators
Immunostimulants
(use of substituted dideoxyimino-D-glucitol compds. for treating **hepatitis** virus infections and combination with other **antiviral** agents or immunostimulants)
- IT **Hepatitis**
(**viral**; use of substituted dideoxyimino-D-glucitol compds. for treating **hepatitis** virus infections and combination with other **antiviral** agents or immunostimulants)
- IT 81117-35-3
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(use of substituted dideoxyimino-D-glucitol compds. for treating **hepatitis** virus infections and combination with other **antiviral** agents or immunostimulants)
- IT 72599-27-0P 131262-77-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(use of substituted dideoxyimino-D-glucitol compds. for treating **hepatitis** virus infections and combination with other **antiviral** agents or immunostimulants)
- IT 3056-17-5, Stavudine 5536-17-4, Ara-A 7481-89-2, Dideoxycytidine 19130-96-2D, 1,5-Dideoxy-1,5-imino-D-glucitol, compds. 25526-93-6 29984-33-6, Ara-AMP 30516-87-1, 3'-Azido-3'-deoxythymidine 36791-04-5

39809-25-1, Penciclovir 59277-89-3, Acyclovir 66341-18-2, Acyclovir triphosphate 69123-90-6, FIAC 69123-98-4, FIAU 69256-17-3, FMAU 69655-05-6, DdI 72599-27-0D, acyl derivs. 73243-67-1 77222-61-8, E-5-(2-Bromovinyl)-2'-deoxyuridine triphosphate 79570-63-1 82410-32-0, Gancyclovir 85326-06-3, 2',3'-Dideoxyguanosine 87190-81-6 91840-92-5 104227-87-4, Famciclovir 106941-25-7, PMEBA 111687-37-7, D-Carbocyclic-2'-deoxyguanosine 115249-95-1 125835-55-4 128985-16-0 131167-83-4 131262-75-4 131262-91-4 134678-17-4, 3TC 143491-54-7, FTC 143698-32-2 143698-33-3 145417-33-0 147058-39-7 211987-43-8 288301-59-7 288301-60-0 288301-61-1 288301-62-2 288301-63-3 288301-64-4 288301-65-5 288301-66-6 288301-67-7 288301-68-8 288301-69-9 288301-70-2 288301-71-3 288301-72-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of substituted dideoxyimino-D-glucitol compds. for treating hepatitis virus infections and combination with other antiviral agents or immunostimulants)

IT 123-72-8, Butyraldehyde 19130-96-2, 1,5-Dideoxy-1,5-imino-D-glucitol RL: RCT (Reactant); RACT (Reactant or reagent)

(use of substituted dideoxyimino-D-glucitol compds. for treating hepatitis virus infections and combination with other antiviral agents or immunostimulants)

IT 69123-90-6, FIAC 79570-63-1 147058-39-7

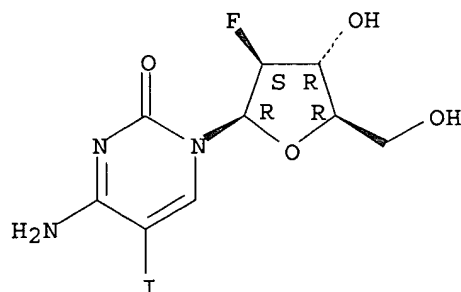
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of substituted dideoxyimino-D-glucitol compds. for treating hepatitis virus infections and combination with other antiviral agents or immunostimulants)

RN 69123-90-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-5-iodo- (9CI) (CA INDEX NAME)

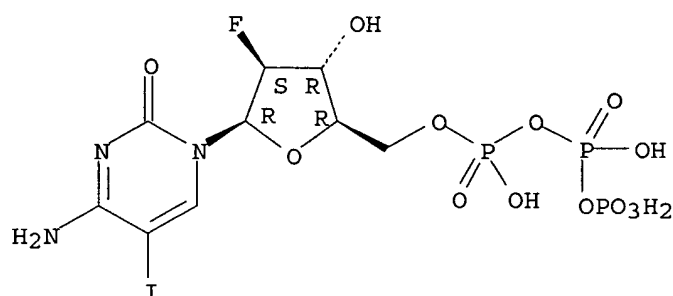
Absolute stereochemistry.



RN 79570-63-1 HCAPLUS

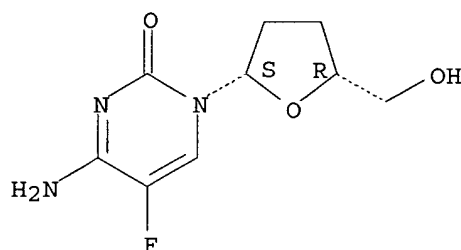
CN 2(1H)-Pyrimidinone, 4-amino-1-[2-deoxy-2-fluoro-5-O-[[hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-β-D-arabinofuranosyl]-5-iodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 147058-39-7 HCAPLUS
CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L34 ANSWER 31 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STM

ACCESSION NUMBER: 2000:314706 HCAPLUS

DOCUMENT NUMBER: 132:308603

TITLE: Preparation of nucleosides with anti-*hepatitis*
B virus activity

INVENTOR(S): Gosselin, Gilles; Imbach, Jean-Louis; Sommadossi,
Jean-Pierre; Schinazi, Raymond F.

PATENT ASSIGNEE(S): Centre National de la Recherche Scientifique, Fr.; The
UAB Research Foundation; Emory University

SOURCE: PCT Int. Appl., 57 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

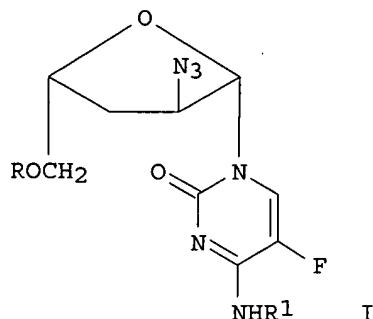
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000026225	A2	20000511	WO 1999-US26157	19991105
WO 2000026225	A3	20001005		
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

CA 2348470	AA	20000511	CA 1999-2348470	19991105
EP 1124839	A2	20010822	EP 1999-958793	19991105
EP 1124839	B1	20060111		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY				
BR 9915555	A	20020115	BR 1999-15555	19991105
US 6458773	B1	20021001	US 1999-435261	19991105
AU 774720	B2	20040708	AU 2000-16085	19991105
RU 2237479	C2	20041010	RU 2001-115094	19991105
AT 315574	E	20060215	AT 1999-958793	19991105
HK 1036069	A1	20060602	HK 2001-106816	20010927
PRIORITY APPLN. INFO.:			US 1998-107116P	P 19981105
			US 1999-115653P	P 19990113
			WO 1999-US26157	W 19991105
OTHER SOURCE(S):	MARPAT 132:308603			
GI				



AB This invention is directed towards the preparation of β -L-(2' or 3'-azido)-2',3'-dideoxy-5-fluorocytosines I (R = H, acyl, monophosphate, diphosphate, triphosphate, or a stabilized phosphate derivative (to form a stabilized nucleotide prodrug); R1 = H, acyl, or alkyl) active against **hepatitis B** virus and a method for the treatment of **hepatitis B** virus infection in humans and other host animals. Thus, β -L-(2'-azido)-2',3'-dideoxy-5-fluorocytidine was prepared and tested for its anti-**hepatitis B** activity in transfected Hep G-2(2.2.15) cells (EC50 = 0.1 μ M) and cytotoxicity (CC50 > 200 μ M).

IC ICM C07H019-00

CC 33-9 (Carbohydrates)

Section cross-reference(s): 1

ST prodrug deoxyerythropentofuranosyl nucleoside prepn **antiviral** cytotoxicity; azidodeoxy fluorocytidine prepn **hepatitis B** treatment **antiviral**; deoxyerythropentofuranonucleoside prepn **hepatitis B** treatment **antiviral**; deoxynucleoside prepn **hepatitis B** treatment virucide

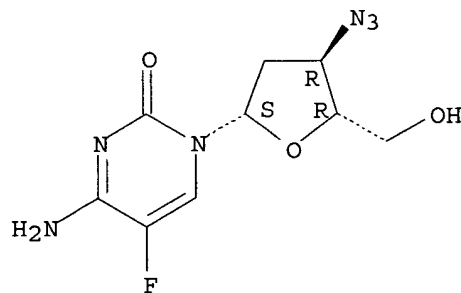
IT **Hepatitis**
(B; preparation of nucleosides with anti-**hepatitis B** virus activity)

IT **Antiviral** agents
Cytotoxicity
(preparation of nucleosides with anti-**hepatitis B** virus activity)

IT Nucleosides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

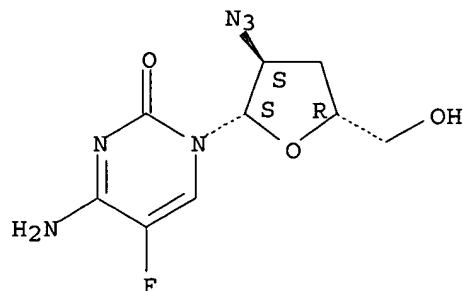
BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of nucleosides with anti-**hepatitis** B virus activity)
 IT Drug delivery systems
 (prodrugs; preparation of nucleosides with anti-**hepatitis** B virus activity)
 IT **265988-73-6P 265988-81-6P**
 RL: **BAC (Biological activity or effector, except adverse)**; BSU
 (Biological study, unclassified); SPN (Synthetic preparation); **THU**
 (**Therapeutic use**); BIOL (Biological study); PREP (Preparation); USES
 (Uses)
 (preparation of nucleosides with anti-**hepatitis** B virus activity)
 IT 51-21-8, 5-Fluorouracil 170079-20-6 201287-82-3
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of nucleosides with anti-**hepatitis** B virus activity)
 IT 77180-89-3P 169823-51-2P 169823-53-4P 265988-66-7P 265988-67-8P
 265988-68-9P 265988-69-0P 265988-70-3P 265988-71-4P 265988-72-5P
 265988-74-7P 265988-75-8P 265988-76-9P 265988-77-0P 265988-78-1P
 265988-79-2P 265988-80-5P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation of nucleosides with anti-**hepatitis** B virus activity)
 IT **265988-73-6P 265988-81-6P**
 RL: **BAC (Biological activity or effector, except adverse)**; BSU
 (Biological study, unclassified); SPN (Synthetic preparation); **THU**
 (**Therapeutic use**); BIOL (Biological study); PREP (Preparation); USES
 (Uses)
 (preparation of nucleosides with anti-**hepatitis** B virus activity)
 RN 265988-73-6 HCAPLUS
 CN 2(1H)-Pyrimidinone, 4-amino-1-(3-azido-2,3-dideoxy- β -L-erythro-
 pentofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 265988-81-6 HCAPLUS
 CN 2(1H)-Pyrimidinone, 4-amino-1-(2-azido-2,3-dideoxy- β -L-erythro-
 pentofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

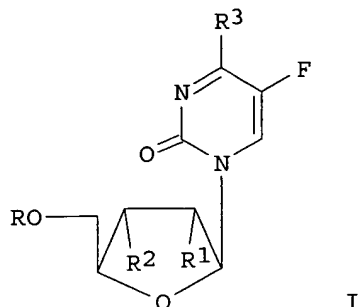
Absolute stereochemistry. Rotation (+).



L34 ANSWER 32 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2000:314558 HCAPLUS
 DOCUMENT NUMBER: 132:308601
 TITLE: Preparation of β -L-2'-deoxy-nucleosides for the treatment of **hepatitis** B virus
 INVENTOR(S): Gosselin, Gilles; Imbach, Jean-Louis; Sommadossi, Jean-Pierre; Schinazi, Raymond F.
 PATENT ASSIGNEE(S): Centre National de la Recherche Scientifique, Fr.; The UAB Research Foundation; Emory University
 SOURCE: PCT Int. Appl., 54 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000025799	A1	20000511	WO 1999-US26156	19991105
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2348948	AA	20000511	CA 1999-2348948	19991105
EP 1124565	A1	20010822	EP 1999-971324	19991105
EP 1124565	B1	20060329		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY				
BR 9915037	A	20011120	BR 1999-15037	19991105
US 6407077	B1	20020618	US 1999-435268	19991105
AU 768059	B2	20031204	AU 2000-14691	19991105
AT 321561	E	20060415	AT 1999-971324	19991105
US 2003036528	A1	20030220	US 2002-175365	20020618
US 6896900	B2	20050524		
AU 2003261475	A1	20031204	AU 2003-261475	20031106
PRIORITY APPLN. INFO.:			US 1998-107178P	P 19981105
			US 1999-115862P	P 19990113
			AU 2000-14691	A3 19991105
			US 1999-435268	A1 19991105
			WO 1999-US26156	W 19991105
OTHER SOURCE(S):		MARPAT 132:308601		

GI



AB Comps. and pharmaceutical compns. active against HIV are provided, as is a method for the treatment of **hepatitis B** virus infection in humans and other host animals is provided comprising administering an effective amount of a β -L-(2' or 3'-azido)-2',3'-dideoxy-5-fluorocytosine of formulas I (R = H, acyl, monophosphate, diphosphate, or triphosphate, or a stabilized phosphate derivative; R1 = N3, R2 = H; R1 = H, R2 = N3; R3 = H, acyl, alkyl). Thus, 1-(3'-azido-2',3'-dideoxy- β -L-erythro-pentofuranosyl)-5-fluorocytosine was prepared and tested in vivo for the treatment of **hepatitis B** virus (EC50 = 0.29 μ M) with cytotoxicity (IC50 > 100 μ M).

IC ICM A61K031-7068

ICS A61P031-18; A61K031-70

CC 33-9 (Carbohydrates)

Section cross-reference(s): 1, 63

ST nucleotide azidodideoxy prepn **antiviral hepatitis B**
treatment AIDS; azidodideoxy nucleoside prepn **antiviral hepatitis B** treatment AIDS; azidodideoxyfluorocytosine prepn **antiviral hepatitis B** treatment

IT AIDS (disease)

Antiviral agents

Hepatitis B virus

(preparation of β -L-2'-deoxy-nucleosides for the treatment of **hepatitis B** virus infection in humans)

IT Nucleosides, preparation

Nucleotides, preparation

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of β -L-2'-deoxy-nucleosides for the treatment of **hepatitis B** virus infection in humans)

IT 265988-73-6P 265988-81-6P 265988-82-7P

265988-83-8P 265988-84-9P 265988-85-0P

265988-86-1P 265988-87-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of β -L-2'-deoxy-nucleosides for the treatment of **hepatitis B** virus infection in humans)

IT 51-21-8, 5-Fluorouracil 1005-56-7, O-Phenyl chlorothionoformate
170079-20-6 201287-82-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of β -L-2'-deoxy-nucleosides for the treatment of
hepatitis B virus infection in humans)

IT 77180-89-3P 169823-51-2P 169823-53-4P 265988-66-7P 265988-67-8P
265988-68-9P 265988-69-0P 265988-70-3P 265988-71-4P 265988-72-5P
265988-74-7P 265988-75-8P 265988-76-9P 265988-77-0P 265988-78-1P
265988-79-2P 265988-80-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(preparation of β -L-2'-deoxy-nucleosides for the treatment of
hepatitis B virus infection in humans)

IT 265988-73-6P 265988-81-6P 265988-82-7P
265988-83-8P 265988-84-9P 265988-85-0P
265988-86-1P 265988-87-2P

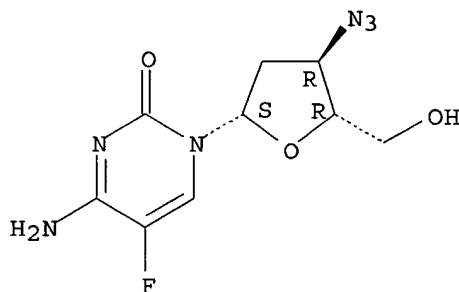
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(preparation of β -L-2'-deoxy-nucleosides for the treatment of
hepatitis B virus infection in humans)

RN 265988-73-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(3-azido-2,3-dideoxy- β -L-erythro-
pentofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

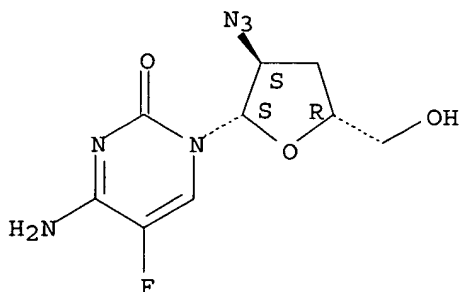
Absolute stereochemistry. Rotation (-).



RN 265988-81-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-azido-2,3-dideoxy- β -L-erythro-
pentofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

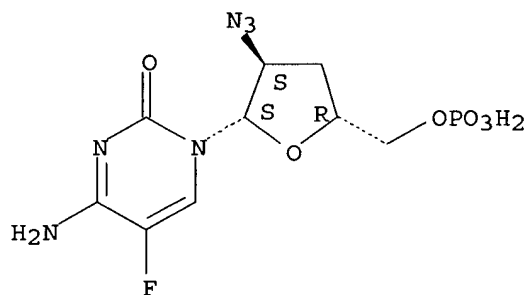


RN 265988-82-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-azido-2,3-dideoxy-5-O-phosphono- β -L-

erythro-pentofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

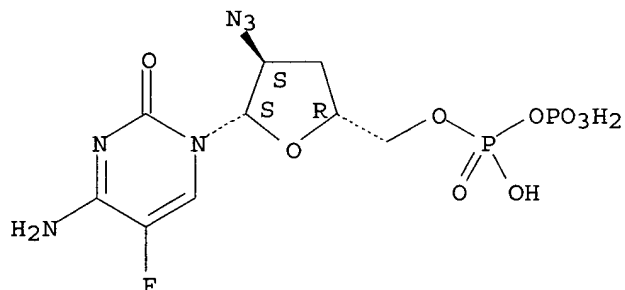
Absolute stereochemistry.



RN 265988-83-8 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-[2-azido-2,3-dideoxy-5-O-[hydroxy(phosphonooxy)phosphinyl]-β-L-erythro-pentofuranosyl]-5-fluoro- (9CI) (CA INDEX NAME)

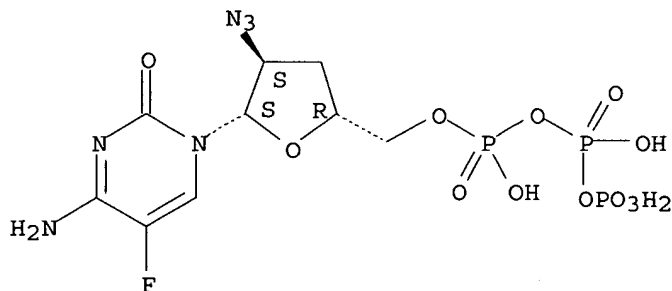
Absolute stereochemistry.



RN 265988-84-9 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-[2-azido-2,3-dideoxy-5-O-[hydroxy[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-β-L-erythro-pentofuranosyl]-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

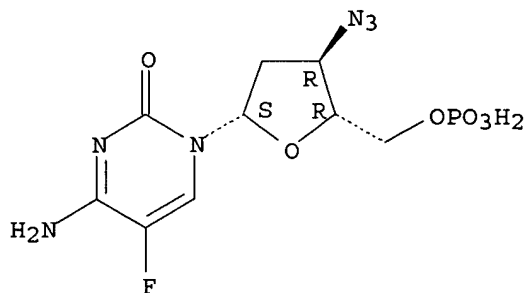


RN 265988-85-0 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(3-azido-2,3-dideoxy-5-O-phosphono-β-L-

erythro-pentofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

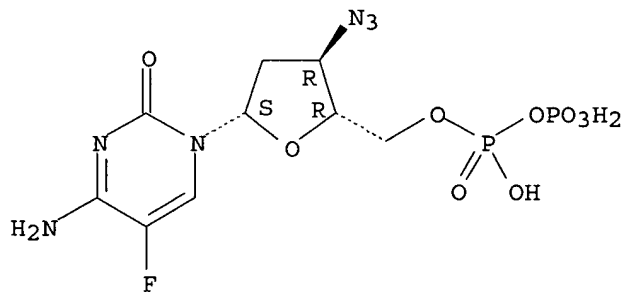
Absolute stereochemistry.



RN 265988-86-1 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-[3-azido-2,3-dideoxy-5-O-[hydroxy(phosphonooxy)phosphinyl]-β-L-erythro-pentofuranosyl]-5-fluoro- (9CI) (CA INDEX NAME)

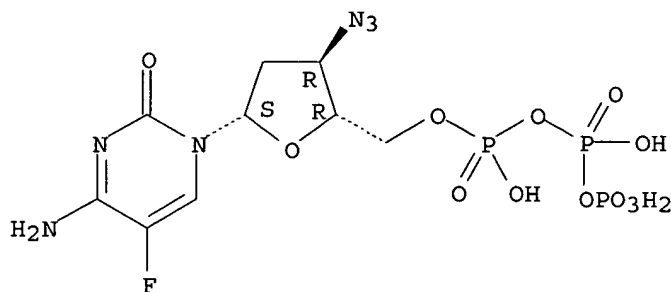
Absolute stereochemistry.



RN 265988-87-2 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-[3-azido-2,3-dideoxy-5-O-[hydroxy[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-β-L-erythro-pentofuranosyl]-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 33 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:255805 HCAPLUS

DOCUMENT NUMBER: 133:83920

TITLE: Synthesis and **antiviral** evaluation of some β -l-2',3'-dideoxy-5-chloropyrimidine nucleosides and pronucleotides

AUTHOR(S): Pierra, C.; Imbach, J.-L.; De Clercq, E.; Balzarini, J.; Van Aerschot, A.; Herdewijn, P.; Faraj, A.; Loi, A. G.; Sommadossi, J.-P.; Gosselin, G.

CORPORATE SOURCE: Laboratoire de Chimie Organique Biomoléculaire de Synthèse, UMR CNRS 5625, Université Montpellier II, Montpellier, 34095, Fr.

SOURCE: Antiviral Research (2000), 45(3), 169-183

CODEN: ARSRDR; ISSN: 0166-3542

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The synthesis and in vitro anti human immunodeficiency virus (HIV) and anti-**hepatitis** B virus (HBV) activities of some unnatural β -l-nucleoside enantiomers related to the anti-HIV compound 2',3'-dideoxy-3'-fluoro-5-chlorouridine (β -d-3'Fdd5ClU) are reported. In contrast to β -d-3'Fdd5ClU, β -l-3'Fdd5ClU and the other l-congeners were devoid of significant anti-HIV effects, but β -l-2',3'-dideoxy-5-chlorocytidine (β -l-dd5ClC) and β -l-2',3'-dideoxy-3'-fluoro-cytidine (β -l-3'FddC) showed a distinct anti-HBV activity. Three mononucleoside phosphotriester derivs. with S-pivaloyl-2-thioethyl (t-BuSATE) groups as biolabile phosphate protective groups were also synthesized. The bis(t-BuSATE) derivative of β -d-3'Fdd5ClU retained anti-HIV activity in thymidine kinase deficient (TK-) CEM cells.

CC 1-5 (Pharmacology)

ST dideoxychloropyrimidine nucleoside pronucleotide **antiviral** antiAIDS prepn; **hepatitis** B virus dideoxychloropyrimidine nucleoside HIV

IT Anti-AIDS agents

Antiviral agents

Hepatitis B virus

Human immunodeficiency virus 1

Human immunodeficiency virus 2

(synthesis and **antiviral** evaluation of β -l-2',3'-dideoxy-5-chloropyrimidine nucleosides and pronucleotides)

IT 177365-15-0P 280564-12-7P

RL: **BAC** (**Biological activity or effector, except adverse**); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); **THU** (**Therapeutic use**); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(synthesis and **antiviral** evaluation of β -l-2',3'-dideoxy-5-chloropyrimidine nucleosides and pronucleotides)

IT 119644-22-3

RL: **BAC** (**Biological activity or effector, except adverse**); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)

(synthesis and **antiviral** evaluation of β -l-2',3'-dideoxy-5-chloropyrimidine nucleosides and pronucleotides)

IT 160963-15-5P 177365-14-9P 280564-23-0P 280564-25-2P 280564-27-4P

RL: **BAC** (**Biological activity or effector, except adverse**); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU**

(**Therapeutic use**); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis and **antiviral** evaluation of β -l-2',3'-dideoxy-5-chloropyrimidine nucleosides and pronucleotides)

IT 9002-06-6, Thymidine kinase

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(synthesis and **antiviral** evaluation of β -l-2',3'-dideoxy-5-chloropyrimidine nucleosides and pronucleotides)

IT 78-67-1 999-97-3, Hexamethyldisilazane 1005-56-7 1820-81-1, 5-Chlorouracil 168777-55-7

RL: RCT (Reactant); RACT (Reactant or reagent)

(synthesis and **antiviral** evaluation of β -l-2',3'-dideoxy-5-chloropyrimidine nucleosides and pronucleotides)

IT 201287-82-3P 280563-97-5P 280564-00-3P 280564-03-6P 280564-08-1P 280564-10-5P 280564-14-9P 280564-18-3P 280564-20-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis and **antiviral** evaluation of β -l-2',3'-dideoxy-5-chloropyrimidine nucleosides and pronucleotides)

IT 280565-84-6P

RL: SPN (Synthetic preparation); PREP (Preparation)

(synthesis and **antiviral** evaluation of β -l-2',3'-dideoxy-5-chloropyrimidine nucleosides and pronucleotides)

IT 177365-15-0P

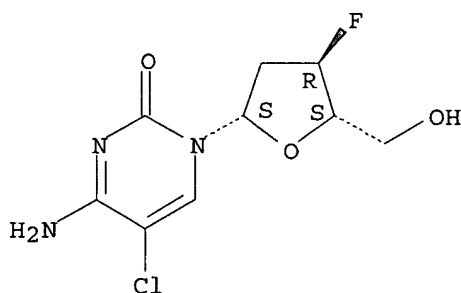
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(synthesis and **antiviral** evaluation of β -l-2',3'-dideoxy-5-chloropyrimidine nucleosides and pronucleotides)

RN 177365-15-0 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-chloro-1-(2,3-dideoxy-3-fluoro- β -L-erythro-pentofuranosyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 160963-15-5P 280564-27-4P

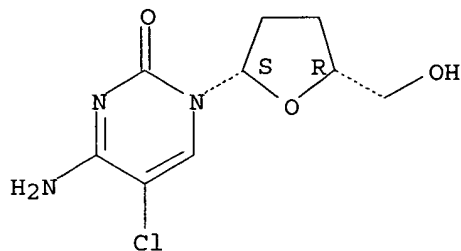
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis and **antiviral** evaluation of β -l-2',3'-dideoxy-5-chloropyrimidine nucleosides and pronucleotides)

RN 160963-15-5 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-chloro-1-[(2S,5R)-2-fluoro-3-hydroxy-5-(4-amino-5-chloro-2-pyrimidinyl)-2-furanyl]- (9CI) (CA INDEX NAME)

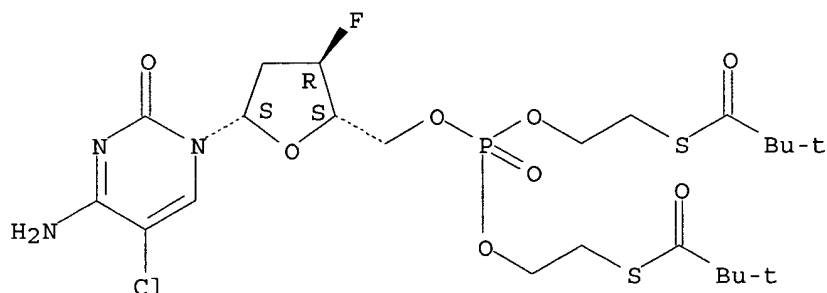
Absolute stereochemistry. Rotation (-).



RN 280564-27-4 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-[5-O-[bis[2-[(2,2-dimethyl-1-oxopropyl)thio]ethoxy]phosphinyl]-2,3-dideoxy-3-fluoro-beta-L-erythro-pentofuranosyl]-5-chloro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 34 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:566061 HCAPLUS

DOCUMENT NUMBER: 131:170587

TITLE: Preparation of 2'-fluoro nucleosides as **antiviral** agents

INVENTOR(S): Schinazi, Raymond F.; Liotta, Dennis C.; Chu, Chung K.; Mcate, J. Jeffrey; Shi, Junxing; Choi, Yongseok; Lee, Kyeong; Hong, Joon H.

PATENT ASSIGNEE(S): Emory University, USA; The University of Georgia Research Foundation, Inc.

SOURCE: PCT Int. Appl., 109 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943691	A1	19990902	WO 1999-US4051	19990225
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS,				

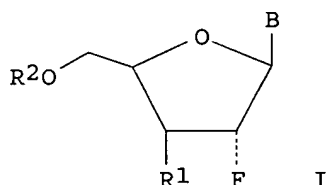
LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,
 SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
 ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
 CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2322008	AA	19990902	CA 1999-2322008	19990225
AU 9927871	A1	19990915	AU 1999-27871	19990225
EP 1058686	A1	20001213	EP 1999-908437	19990225
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, RO				
JP 2002504558	T2	20020212	JP 2000-533443	19990225
US 6348587	B1	20020219	US 1999-257130	19990225
BR 9908270	A	20040629	BR 1999-8270	19990225
US 2002198171	A1	20021226	US 2002-61128	20020130
US 6911424	B2	20050628		
AU 2003244569	A1	20031002	AU 2003-244569	20030905
US 2004254141	A1	20041216	US 2004-796529	20040308

PRIORITY APPLN. INFO.:

US 1998-75893P	P	19980225
US 1998-80569P	P	19980403
US 1999-257130	A1	19990225
WO 1999-US4051	W	19990225
US 2002-61128	A1	20020130

OTHER SOURCE(S): MARPAT 131:170587
 GI



AB 2'-Fluoro nucleoside compds. I wherein R1 is OH, H, OR3, N3, CN, halogen, including F, or CF3, lower alkyl, amino, lower alkylamino, or alkoxy, and base refers to a purine or pyrimidine base; R2 is H, phosphate, including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug; acyl, or other pharmaceutically acceptable leaving group which when administered in vivo, is capable of providing a compound wherein R2 is H or phosphate; sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl, benzyl, wherein the Ph group is optionally substituted with one or more substituents as described in the definition of aryl given above, a lipid, an amino acid, peptide, or cholesterol; and R3 is acyl, alkyl, phosphate, or other pharmaceutically acceptable leaving group which when administered in vivo, is capable of being cleaved to the parent compound, or a pharmaceutically acceptable salt thereof, are disclosed which are useful in the treatment of **hepatitis B** infection, **hepatitis C** infection, HIV and abnormal cellular proliferation, including tumors and cancer. Thus, 1-(2,3-dideoxy-2-fluoro-β-L-glycero-pent-2-eno-furanosyl)thymine was prepared and tested for its **antiviral** activity (EC50 > 100 μM).

IC ICM C07H019-06

ICS C07H019-10; C07H019-16; C07H019-20; C07H019-207; C07D473-00;
 C07D405-04; C07F009-547; A61K031-70

CC 33-9 (Carbohydrates)

Section cross-reference(s): 1, 63

ST antitumor fluoro nucleoside prepn **antiviral**; fluoro nucleoside
prepn **antiviral** proliferation inhibitor

IT Antitumor agents
Antiviral agents
Cytotoxic agents
(preparation of fluoro nucleosides as **antiviral** agents and
proliferation inhibitors)

IT Nucleosides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fluoro nucleosides as **antiviral** agents and
proliferation inhibitors)

IT Proliferation inhibition
(proliferation inhibitors; preparation of fluoro nucleosides as
antiviral agents and proliferation inhibitors)

IT 121353-93-3P 122929-23-1P 169835-86-3P 181785-91-1P 202272-20-6P
202272-21-7P 202272-22-8P 202272-23-9P 202272-24-0P
202272-25-1P 202272-26-2P 202272-33-1P 202272-34-2P
202272-35-3P 202272-36-4P 202272-37-5P 202272-38-6P
210474-65-0P 210474-68-3P 210474-73-0P 210474-75-2P 212954-60-4P
212964-24-4P 212964-25-5P 221156-34-9P 221617-05-6P 221617-08-9P
221617-16-9P 221617-18-1P 221662-48-2P 221662-49-3P 221662-50-6P
221662-51-7P 222974-41-6P
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); SPN (Synthetic preparation); **THU**
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(preparation of fluoro nucleosides as **antiviral** agents and
proliferation inhibitors)

IT 9068-38-6, Reverse transcriptase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
(preparation of fluoro nucleosides as **antiviral** agents and
proliferation inhibitors)

IT 51-21-8, 5-FluoroUracil 65-71-4, Thymine 66-22-8, Uracil, reactions
68-94-0, Hypoxanthine 71-30-7, Cytosine 73-24-5, Adenine, reactions
73-40-5, Guanine 87-42-3, 6-Chloropurine 554-01-8, 5-Methylcytosine
1128-23-0 1904-98-9, 2,6-Diaminopurine 2356-16-3 3195-24-2
128075-94-5 133745-75-2 152963-76-3 170079-96-6 202272-27-3
238747-27-8 238747-36-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of fluoro nucleosides as **antiviral** agents and
proliferation inhibitors)

IT 18325-74-1P 21622-01-5P 22323-80-4P 25125-21-7P,
3-Cyclopentene-1-methanol 72598-06-2P 94697-68-4P 137836-41-0P
169835-84-1P 202272-16-0P 202272-17-1P 202272-18-2P 202272-19-3P
202272-28-4P 202272-29-5P 202272-30-8P 202272-31-9P 202272-32-0P
210474-35-4P 210474-45-6P 210474-50-3P 210474-52-5P 210474-57-0P
210474-60-5P 221156-33-8P 221156-52-1P 221156-53-2P 221156-54-3P
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221616-83-7P 221616-85-9P 221616-90-6P 221616-91-7P 221616-93-9P
221616-94-0P 221616-95-1P 221616-97-3P 221617-12-5P 221617-14-7P
238747-28-9P 238747-29-0P 238747-42-7P 238747-44-9P 238747-47-2P
238747-49-4P 238747-51-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of fluoro nucleosides as **antiviral** agents and
proliferation inhibitors)

IT 202272-21-7P 202272-25-1P 202272-35-3P
202272-38-6P

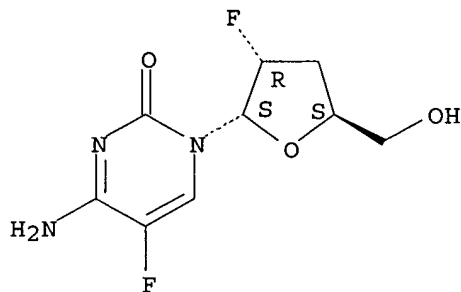
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(preparation of fluoro nucleosides as **antiviral** agents and
proliferation inhibitors)

RN 202272-21-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2,3-dideoxy-2-fluoro- α -D-erythro-
pentofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

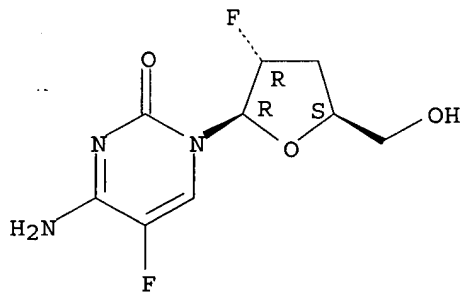
Absolute stereochemistry.



RN 202272-25-1 HCAPLUS

CN Cytidine, 2',3'-dideoxy-2',5-difluoro- (9CI) (CA INDEX NAME)

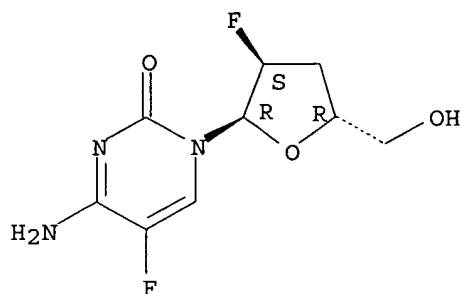
Absolute stereochemistry.



RN 202272-35-3 HCAPLUS

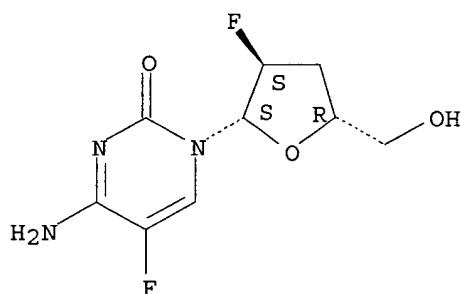
CN 2(1H)-Pyrimidinone, 4-amino-1-(2,3-dideoxy-2-fluoro- α -L-erythro-
pentofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 202272-38-6 HCAPLUS
 CN 2(1H)-Pyrimidinone, 4-amino-1-(2,3-dideoxy-2-fluoro- β -L-erythro-pentofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 35 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1999:529023 HCAPLUS
 DOCUMENT NUMBER: 131:165293
 TITLE: Use of N-substituted-1,5-dideoxy-1,5-imino-D-glucitol compounds for treating *hepatitis* virus infections
 INVENTOR(S): Mueller, Richard A.; Bryant, Martin L.; Partis, Richard A.
 PATENT ASSIGNEE(S): G.D. Searle and Co., USA
 SOURCE: PCT Int. Appl., 138 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9940916	A1	19990819	WO 1999-US1874	19990212
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2003100532	A1	20030529	US 1998-23401	19980212
CA 2319713	AA	19990819	CA 1999-2319713	19990212
AU 9927595	A1	19990830	AU 1999-27595	19990212
AU 762125	B2	20030619		
ZA 9901142	A	20000214	ZA 1999-1142	19990212
BR 9907882	A	20001017	BR 1999-7882	19990212
TR 200002323	T2	20001221	TR 2000-200002323	19990212
EP 1061922	A1	20001227	EP 1999-908079	19990212
EP 1061922	B1	20060628		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI

JP 2002502875	T2	20020129	JP 2000-531168	19990212
CN 1679568	A	20051012	CN 2005-10062642	19990212
TW 222867	B1	20041101	TW 1999-88102296	19990407
AU 2003248024	A1	20031030	AU 2003-248024	20030918
US 2006094671	A1	20060504	US 2005-300464	20051215
US 2006106065	A1	20060518	US 2005-300463	20051215

PRIORITY APPLN. INFO.:

US 1998-23401	A	19980212
US 1998-74508P	P	19980212
US 1997-41221P	P	19970214
CN 1999-804990	A3	19990212
WO 1999-US1874	W	19990212

OTHER SOURCE(S): MARPAT 131:165293

AB Methods and compns. are provided for treating **hepatitis** virus infections in mammals, especially humans. The methods comprise (1) administering N-substituted-1,5-dideoxy-1,5-imino-D-glucitol compds. alone or in combination with nucleoside **antiviral** agents, nucleotide **antiviral** agents, mixts. thereof, or immunomodulating/immunostimulating agents, or (2) administering N-substituted-1,5-dideoxy-1,5-imino-D-glucitol compds. alone or in combination with nucleoside **antiviral** agents, nucleotide **antiviral** agents, or mixts. thereof, and immunomodulating/immunostimulating agents.

IC ICM A61K031-445

CC 1-5 (Pharmacology)

Section cross-reference(s): 27, 63

ST dideoxyiminoglucitol deriv **hepatitis antiviral**;
nucleoside dideoxyiminoglucitol deriv combination **antiviral hepatitis**; nucleotide dideoxyiminoglucitol deriv combination **antiviral hepatitis**; immunomodulator dideoxyiminoglucitol deriv combination **antiviral hepatitis**; immunostimulant dideoxyiminoglucitol deriv combination **antiviral hepatitis**

IT **Antiviral** agents

Drug delivery systems

Hepatitis B virus

Hepatitis virus

Immunomodulators

Immunostimulants

(N-substituted-1,5-dideoxy-1,5-imino-D-glucitol compds., alone or with other agents, for treating **hepatitis** virus infections)

IT Nucleoside analogs

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(N-substituted-1,5-dideoxy-1,5-imino-D-glucitol compds., alone or with other agents, for treating **hepatitis** virus infections)

IT Nucleosides, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(acidic moiety-containing, dideoxyiminoglucitol derivative salts; N-substituted-1,5-dideoxy-1,5-imino-D-glucitol compds., alone or with other agents, for treating **hepatitis** virus infections)

IT Nucleotides, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(analog; N-substituted-1,5-dideoxy-1,5-imino-D-glucitol compds., alone or with other agents, for treating **hepatitis** virus infections)

IT Nucleotides, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(dideoxyiminoglucitol derivative salts; N-substituted-1,5-dideoxy-1,5-imino-D-glucitol compds., alone or with other agents, for treating **hepatitis** virus infections)

IT Drug interactions

(synergistic; N-substituted-1,5-dideoxy-1,5-imino-D-glucitol compds., alone or with other agents, for treating **hepatitis** virus infections)

IT 72599-27-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(N-substituted-1,5-dideoxy-1,5-imino-D-glucitol compds., alone or with other agents, for treating **hepatitis** virus infections)

IT 81117-35-3 134678-17-4, 3TC

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)

(N-substituted-1,5-dideoxy-1,5-imino-D-glucitol compds., alone or with other agents, for treating **hepatitis** virus infections)

IT 131262-77-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(N-substituted-1,5-dideoxy-1,5-imino-D-glucitol compds., alone or with other agents, for treating **hepatitis** virus infections)

IT 3056-17-5, Stavudine 5536-17-4, Ara-A 7481-89-2 19130-96-2D, 1,5-Dideoxy-1,5-imino-D-glucitol, derivs. 25526-93-6 29984-33-6, Ara-AMP 29984-33-6D, Ara-AMP, dideoxyiminoglucitol derivative salts 30516-87-1, AZT 36791-04-5 39809-25-1, Penciclovir 59277-89-3, Acyclovir 66341-18-2, Acyclovir triphosphate 66341-18-2D, Acyclovir triphosphate, dideoxyiminoglucitol derivative salts **69123-90-6**, FIAC 69123-98-4, FIAU 69256-17-3, FMAU 69256-17-3D, dideoxyiminoglucitol derivative salts 69655-05-6, Dideoxyinosine 72458-45-8 72458-45-8D, salts with acidic moiety-containing nucleosides and nucleotides 72458-46-9 72458-46-9D, salts with acidic moiety-containing nucleosides and nucleotides 73243-67-1 73243-67-1D, salts with acidic moiety-containing nucleosides and nucleotides 77222-61-8 77222-61-8D, dideoxyiminoglucitol derivative salts 79206-10-3 79206-10-3D, salts with acidic moiety-containing nucleosides and nucleotides 79206-12-5 79206-12-5D, salts with acidic moiety-containing nucleosides and nucleotides 79206-14-7 79206-14-7D, salts with acidic moiety-containing nucleosides and nucleotides 79206-20-5 79206-20-5D,

salts with acidic moiety-containing nucleosides and nucleotides 79206-22-7
79206-22-7D, salts with acidic moiety-containing nucleosides and nucleotides
81117-35-3D, salts with acidic moiety-containing nucleosides and nucleotides
81117-36-4 81117-36-4D, salts with acidic moiety-containing nucleosides and
nucleotides 81117-38-6 81117-38-6D, salts with acidic moiety-containing
nucleosides and nucleotides 82410-32-0 85326-06-3 87190-81-6
100018-53-9 104227-87-4, Famciclovir 106941-25-7, PMEA 115183-38-5
115183-38-5D, salts with acidic moiety-containing nucleosides and nucleotides
115249-95-1 121154-51-6 128985-11-5 128985-11-5D, salts with acidic
moiety-containing nucleosides and nucleotides 131167-83-4 131262-82-3
131262-91-4 131262-93-6 134678-17-4D, 3TC, dideoxyiminoglucitol derivative
salts 137530-41-7 143491-54-7, FTC 145417-33-0 **147058-39-7**
159119-82-1 160632-03-1 160632-03-1D, salts with acidic moiety-containing
nucleosides and nucleotides 160632-05-3 160632-05-3D, salts with
acidic moiety-containing nucleosides and nucleotides 160963-03-1
162398-48-3 162398-48-3D, salts with acidic moiety-containing nucleosides
and nucleotides 162398-56-3 162398-56-3D, salts with acidic
moiety-containing nucleosides and nucleotides 211987-28-9 211987-28-9D,
salts with acidic moiety-containing nucleosides and nucleotides 211987-29-0
211987-29-0D, salts with acidic moiety-containing nucleosides and nucleotides
211987-30-3 211987-30-3D, salts with acidic moiety-containing nucleosides
and nucleotides 211987-31-4 211987-31-4D, salts with acidic
moiety-containing nucleosides and nucleotides 211987-32-5 211987-32-5D,
salts with acidic moiety-containing nucleosides and nucleotides 211987-33-6
211987-33-6D, salts with acidic moiety-containing nucleosides and nucleotides
211987-34-7 211987-34-7D, salts with acidic moiety-containing nucleosides
and nucleotides 211987-35-8 211987-35-8D, salts with acidic
moiety-containing nucleosides and nucleotides 211987-36-9 211987-36-9D,
salts with acidic moiety-containing nucleosides and nucleotides 211987-37-0
211987-37-0D, salts with acidic moiety-containing nucleosides and nucleotides
211987-38-1 211987-38-1D, salts with acidic moiety-containing nucleosides
and nucleotides 211987-39-2 211987-39-2D, salts with acidic
moiety-containing nucleosides and nucleotides 211987-40-5 211987-40-5D,
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211987-41-6D, salts with acidic moiety-containing nucleosides and nucleotides
211987-42-7 211987-42-7D, salts with acidic moiety-containing nucleosides
and nucleotides 211987-43-8 211987-43-8D, salts with acidic
moiety-containing nucleosides and nucleotides 211987-44-9 211987-44-9D,
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211987-45-0D, salts with acidic moiety-containing nucleosides and nucleotides
211987-46-1 211987-46-1D, salts with acidic moiety-containing nucleosides
and nucleotides 211987-47-2 211987-47-2D, salts with acidic
moiety-containing nucleosides and nucleotides 211987-48-3 211987-48-3D,
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211987-49-4D, salts with acidic moiety-containing nucleosides and nucleotides
211987-50-7 211987-50-7D, salts with acidic moiety-containing nucleosides
and nucleotides 211987-51-8 211987-51-8D, salts with acidic
moiety-containing nucleosides and nucleotides 211987-52-9 211987-52-9D,
salts with acidic moiety-containing nucleosides and nucleotides 211987-53-0
211987-53-0D, salts with acidic moiety-containing nucleosides and nucleotides
211987-54-1 211987-54-1D, salts with acidic moiety-containing nucleosides
and nucleotides 211987-55-2 211987-55-2D, salts with acidic
moiety-containing nucleosides and nucleotides 211987-56-3 211987-56-3D,
salts with acidic moiety-containing nucleosides and nucleotides 211987-57-4
211987-57-4D, salts with acidic moiety-containing nucleosides and nucleotides
211987-58-5 211987-58-5D, salts with acidic moiety-containing nucleosides
and nucleotides 211987-59-6 211987-59-6D, salts with acidic
moiety-containing nucleosides and nucleotides 211987-60-9 211987-60-9D,
salts with acidic moiety-containing nucleosides and nucleotides 211987-61-0

211987-61-0D, salts with acidic moiety-containing nucleosides and nucleotides
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 and nucleotides 223771-90-2 223771-90-2D, salts with acidic
 moiety-containing nucleosides and nucleotides 223772-09-6 223772-09-6D,
 salts with acidic moiety-containing nucleosides and nucleotides 238075-04-2
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 238075-05-3 238075-05-3D, salts with acidic moiety-containing nucleosides
 and nucleotides 238075-06-4 238075-06-4D, salts with acidic
 moiety-containing nucleosides and nucleotides 238075-07-5 238075-07-5D,
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 238075-08-6D, salts with acidic moiety-containing nucleosides and nucleotides
 238075-09-7 238075-09-7D, salts with acidic moiety-containing nucleosides
 and nucleotides 238075-10-0 238075-10-0D, salts with acidic
 moiety-containing nucleosides and nucleotides 238075-11-1 238075-11-1D,
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 238075-12-2D, salts with acidic moiety-containing nucleosides and nucleotides
 238075-13-3 238075-13-3D, salts with acidic moiety-containing nucleosides
 and nucleotides 238075-14-4 238075-14-4D, salts with acidic
 moiety-containing nucleosides and nucleotides 238075-15-5 238075-15-5D,
 salts with acidic moiety-containing nucleosides and nucleotides 238075-16-6
 238075-16-6D, salts with acidic moiety-containing nucleosides and nucleotides
 238075-17-7 238075-17-7D, salts with acidic moiety-containing nucleosides
 and nucleotides 238075-18-8 238075-18-8D, salts with acidic
 moiety-containing nucleosides and nucleotides 238075-19-9 238075-19-9D,
 salts with acidic moiety-containing nucleosides and nucleotides 238075-20-2
 238075-20-2D, salts with acidic moiety-containing nucleosides and nucleotides
 238075-21-3 238075-21-3D, salts with acidic moiety-containing nucleosides
 and nucleotides 238075-22-4 238075-22-4D, salts with acidic
 moiety-containing nucleosides and nucleotides

RL: **BAC (Biological activity or effector, except adverse)**; BSU
 (Biological study, unclassified); **THU (Therapeutic use)**; BIOL
 (Biological study); USES (Uses)

(N-substituted-1,5-dideoxy-1,5-imino-D-glucitol compds., alone or with
 other agents, for treating **hepatitis** virus infections)

IT 108-24-7, Acetic anhydride 123-72-8, Butyraldehyde 19130-96-2,
 1,5-Dideoxy-1,5-imino-D-glucitol

RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction; N-substituted-1,5-dideoxy-1,5-imino-D-glucitol compds.,
 alone or with other agents, for treating **hepatitis** virus
 infections)

IT **69123-90-6**, FIAC **147058-39-7**

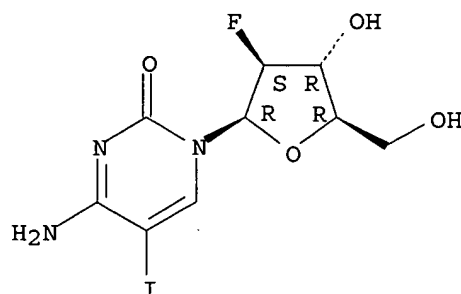
RL: **BAC (Biological activity or effector, except adverse)**; BSU
 (Biological study, unclassified); **THU (Therapeutic use)**; BIOL
 (Biological study); USES (Uses)

(N-substituted-1,5-dideoxy-1,5-imino-D-glucitol compds., alone or with
 other agents, for treating **hepatitis** virus infections)

RN 69123-90-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-
 5-iodo- (9CI) (CA INDEX NAME)

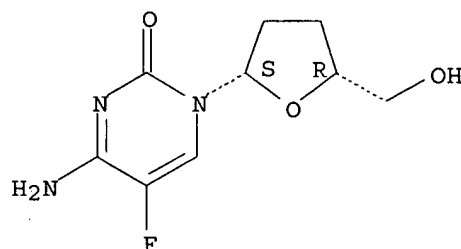
Absolute stereochemistry.



RN 147058-39-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 36 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:117751 HCAPLUS

DOCUMENT NUMBER: 131:220

TITLE: The **hepatitis** B virus-trimera mouse: a model for human HBV infection and evaluation of anti-HBV therapeutic agents

AUTHOR(S): Ilan, Ehud; Burakova, Tatjana; Dagan, Shlomo; Nussbaum, Ofer; Lubin, Ido; Eren, Rachel; Ben-Moshe, Ofer; Arazi, Joseph; Berr, Shoshana; Neville, Lewis; Yuen, Leonard; Mansour, Tarek S.; Gillard, John; Eid, Ahamed; Jurim, Oded; Shouval, Daniel; Reisner, Yair; Galun, Eithan

CORPORATE SOURCE: XTL Biopharmaceuticals Ltd, Rehovot, 76100, Israel

SOURCE: Hepatology (Philadelphia) (1999), 29(2), 553-562

CODEN: HPTLD9; ISSN: 0270-9139

PUBLISHER: W. B. Saunders Co.

DOCUMENT TYPE: Journal

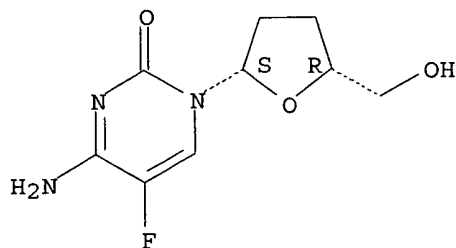
LANGUAGE: English

AB Previous studies have demonstrated the feasibility of implantation of human blood cells or tissues in lethally irradiated mice or rats, radioprotected with SCID mouse bone marrow cells: The Trimera system. In the present study, we describe the development of a mouse Trimera model for human **hepatitis** B virus (HBV) infection. In this model, viremia is induced by transplantation of ex vivo HBV-infected human liver fragments. Engraftment of the human liver fragments, evaluated by hematoxylin-eosin staining and human serum albumin mRNA expression, was

observed in 85% of the transplanted animals 1 mo postimplantation. Viremia levels were determined in these mice by measuring serum HBV DNA using polymerase chain reaction (PCR), followed by dot-blot hybridization. HBV DNA is first detected 8 days after liver transplantation. Viremia attains a peak between days 18 and 25 when HBV infection is observed in 85% of the transplanted animals. The HBV-Trimera model was used to evaluate the therapeutic effects of human polyclonal anti-HBs antibodies (Hepatect) and of two reverse-transcriptase inhibitors, lamivudine (3TC) and β -L-5-fluoro-2',3'-dideoxycytidine (β -L-5FddC). Treatment of HBV-Trimera mice with these drugs effectively reduced both the percentage of infected animals and the viral load in their sera. Treatment cessation resulted in rebound of viral load, indicating HBV replication upon drug withdrawal. These results show that the HBV-Trimera model represents a novel exptl. tool for simulating human HBV infection and evaluating potential anti-HBV therapeutic agents.

CC 1-5 (Pharmacology)
 Section cross-reference(s): 14
 ST **hepatitis** B virus mouse trimera model; HBV infection
antiviral mouse trimera
 IT **Antiviral** agents
 Disease models
Hepatitis B virus
 Mouse
 (antiviral effects anti-HBV therapeutic agents in
hepatitis B virus-trimera mouse model for human HBV infection)
 IT 134678-17-4, Lamivudine 147058-39-7
 RL: **BAC (Biological activity or effector, except adverse)**; BSU
 (Biological study, unclassified); **THU (Therapeutic use)**; BIOL
 (Biological study); USES (Uses)
 (antiviral effects anti-HBV therapeutic agents in
hepatitis B virus-trimera mouse model for human HBV infection)
 IT 147058-39-7
 RL: **BAC (Biological activity or effector, except adverse)**; BSU
 (Biological study, unclassified); **THU (Therapeutic use)**; BIOL
 (Biological study); USES (Uses)
 (antiviral effects anti-HBV therapeutic agents in
hepatitis B virus-trimera mouse model for human HBV infection)
 RN 147058-39-7 HCAPLUS
 CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 37 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1998:568726 HCAPLUS

DOCUMENT NUMBER: 129:197981
 TITLE: Use of N-substituted-1,5-dideoxy-1,5-imino-D-glucitol compounds in combination therapy for treating **hepatitis** virus infections
 INVENTOR(S): Jacob, Gary S.; Block, Timothy M.; Dwek, Raymond A.
 PATENT ASSIGNEE(S): G.D. Searle and Co., USA
 SOURCE: PCT Int. Appl., 74 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9835685	A1	19980820	WO 1998-US3004	19980212
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9861692	A1	19980908	AU 1998-61692	19980212
EP 1007058	A1	20000614	EP 1998-906475	19980212
EP 1007058	B1	20050518		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2001512462	T2	20010821	JP 1998-535987	19980212
AT 295732	E	20050615	AT 1998-906475	19980212
ES 2244048	T3	20051201	ES 1998-906475	19980212
US 6689759	B1	20040210	US 2000-355446	20000119
US 2006094671	A1	20060504	US 2005-300464	20051215
US 2006106065	A1	20060518	US 2005-300463	20051215
PRIORITY APPLN. INFO.:			US 1997-41221P	P 19970214
			US 1998-23401	B1 19980212
			WO 1998-US3004	W 19980212

OTHER SOURCE(S): MARPAT 129:197981

AB Methods and compns. are provided for treating **hepatitis** virus infections in mammals, especially humans. The methods comprise (1) administering N-substituted-1,5-dideoxy-1,5-imino-D-glucitol compds. in combination with nucleoside **antiviral** agents, nucleotide **antiviral** agents, mixts. thereof, or immunomodulating/immunostimulating agents, or (2) administering N-substituted-1,5-dideoxy-1,5-imino-D-glucitol compds. in combination with nucleoside **antivirals** agents, nucleotide **antiviral** agents, or mixts. thereof, and immunomodulating/immunostimulating agents. Preparation of

1,5-(butylimino)-1,5-dideoxy-D-glucitol and of the corresponding tetraacetate is described.

IC ICM A61K031-70
 ICS A61K031-70; A61K031-445

CC 1-5 (Pharmacology)
 Section cross-reference(s): 33, 63

ST dideoxyiminoglucitol deriv **antiviral hepatitis** virus; tetraacetate butyliminodideoxyglucitol prepn **antiviral hepatitis** virus; nucleoside dideoxyiminoglucitol deriv **antiviral** combination **hepatitis**; nucleotide dideoxyiminoglucitol deriv **antiviral** combination **hepatitis**; immunomodulator dideoxyiminoglucitol deriv

**antiviral combination hepatitis; immunostimulant
dideoxyiminoglucitol deriv antiviral combination
hepatitis**

IT Nucleotides, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(analog, **antiviral**; dideoxyiminoglucitol derivs. in combination therapy for treating **hepatitis** virus infections)

IT Nucleoside analogs

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**antiviral**; dideoxyiminoglucitol derivs. in combination therapy for treating **hepatitis** virus infections)

IT **Antiviral agents**

Drug delivery systems

Drug interactions

Hepatitis B virus

Hepatitis virus

(dideoxyiminoglucitol derivs. in combination therapy for treating **hepatitis** virus infections)

IT 3056-17-5, Stavudine 7481-89-2, Dideoxycytidine 19130-96-2D, 1,5-Dideoxy-1,5-imino-D-glucitol, N-substituted derivs. 25526-93-6 30516-87-1, AZT 36791-04-5 66341-18-2, Acyclovir triphosphate 69123-90-6, FIAC 69256-17-3 69655-05-6, Dideoxyinosine 72458-45-8 72458-46-9 73243-67-1 79206-10-3 79206-12-5 79206-20-5 79206-22-7 80860-82-8 81117-34-2 81117-35-3 81117-38-6 85326-06-3 87190-81-6 99876-43-4 106941-25-7, 9-(2-Phosphonylmethoxyethyl)adenine 111687-37-7, D-Carbocyclic-2'-deoxyguanosine 115249-95-1 121154-51-6 128985-11-5 131167-83-4 134678-17-4, 3TC 134680-32-3 137530-41-7 143491-54-7, FTC 147058-39-7 160963-03-1 211987-28-9 211987-29-0 211987-30-3 211987-31-4 211987-32-5 211987-33-6 211987-34-7 211987-35-8 211987-36-9 211987-37-0 211987-38-1 211987-39-2 211987-40-5 211987-41-6 211987-42-7 211987-43-8 211987-44-9 211987-45-0 211987-46-1 211987-47-2 211987-48-3 211987-49-4 211987-50-7 211987-51-8 211987-52-9 211987-53-0 211987-54-1 211987-55-2 211987-56-3 211987-57-4 211987-58-5 211987-59-6 211987-60-9 211987-61-0 211987-62-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(dideoxyiminoglucitol derivs. in combination therapy for treating **hepatitis** virus infections)

IT 72599-27-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(dideoxyiminoglucitol derivs. in combination therapy for treating **hepatitis** virus infections, and derivative preparation)

IT 131262-77-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(dideoxyiminoglucitol derivs. in combination therapy for treating **hepatitis** virus infections, and derivative preparation)

IT 108-24-7, Acetic anhydride 123-72-8, Butyraldehyde 19130-96-2,

1,5-Dideoxy-1,5-imino-D-glucitol

RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction; dideoxyiminoglucitol derivs. in combination therapy for treating **hepatitis** virus infections, and derivative preparation)

IT 69123-90-6, FIAC 99876-43-4 147058-39-7

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); THU (Therapeutic use); BIOL

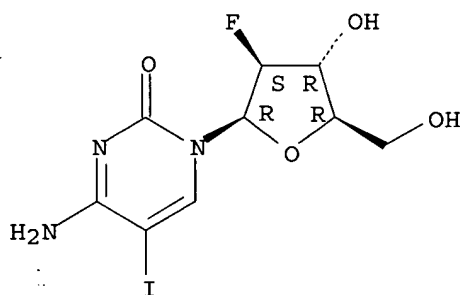
(Biological study); USES (Uses)

(dideoxyiminoglucitol derivs. in combination therapy for treating **hepatitis** virus infections)

RN 69123-90-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-5-iodo- (9CI) (CA INDEX NAME)

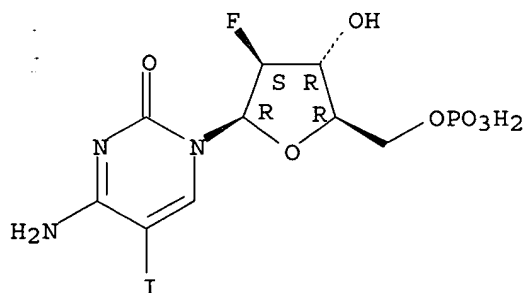
Absolute stereochemistry.



RN 99876-43-4 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy-2-fluoro-5-O-phosphono-β-D-arabinofuranosyl)-5-iodo- (9CI) (CA INDEX NAME)

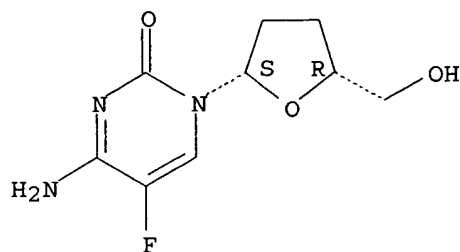
Absolute stereochemistry.



RN 147058-39-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 38 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:553293 HCAPLUS

DOCUMENT NUMBER: 130:10320

TITLE: Inhibition of the replication of *hepatitis* B virus in vitro by β -L-2',3'-bis-deoxy-5-fluorocytidine

AUTHOR(S): Zhu, Yonglian

CORPORATE SOURCE: Department of Pharmacology, Zhejiang Medical University, Hangzhou, 310031, Peop. Rep. China

SOURCE: Zhejiang Yike Daxue Xuebao (1998), 27(3), 97-100
CODEN: ZYDXDM; ISSN: 1000-1743

PUBLISHER: Zhejiang Yike Daxue Xuebao Bianji Weiyuanhui

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB The cytidine class compound 2',3'-bis-deoxy-cytidine (dC) exhibited HBV replication effect, but had the adverse effect with peripheral neuritis because of its inhibition on cell mitochondrial DNA synthesis. HBV DNA replication inhibitive effect of β -L-2',3'-bis-deoxy-5-fluorocytidine (dFC), a dC modified compound, its cytotoxicity to human T-lymphoblastoid (CEM) cells, and the inhibitive effect on CEM mitochondrial DNA synthesis were studied. The HBV DNA IC₅₀ of dC was 4 vs. 0.05 μ mol/L of the dFC, but the inhibition effect of dFC was reversible, replication of HBV DNA recovered to 45% 12 d after the drug was withdrawn. The EC₅₀ on CEM cell growth inhibition of dC and dFC were 28 and 67 μ mol/L, CEM cell mitochondrial DNA synthesis IC₅₀ were 0.07 and >100 μ mol/L, and the selective index of dC and dFC were 7 and 1340 resp. The results suggest that the dFC is obviously superior vs. the original dC above the enhanced **antiviral** activity and attenuated adverse effect in the in vitro study.

CC 1-5 (Pharmacology)

ST *hepatitis* B virus bisdeoxyfluorcytidine DNA cytotoxicity

IT **Hepatitis**

(B; inhibition of the replication of *hepatitis* B virus in vitro by β -L-2',3'-bis-deoxy-5-fluorocytidine)

IT **Antiviral** agents

Cytotoxicity

DNA formation

Mitochondria

T cell (lymphocyte)

(inhibition of the replication of *hepatitis* B virus in vitro by β -L-2',3'-bis-deoxy-5-fluorocytidine)

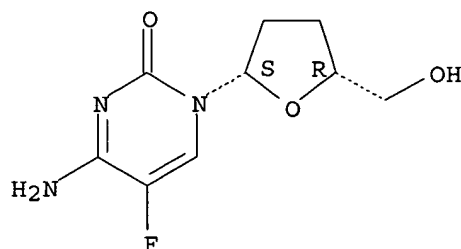
IT DNA formation

(replication; inhibition of the replication of *hepatitis* B virus in vitro by β -L-2',3'-bis-deoxy-5-fluorocytidine)

IT 147058-39-7, β -L-2',3'-Dideoxy-5-fluorocytidine

RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); USES (Uses)
(inhibition of the replication of **hepatitis B** virus in vitro
by β -L-2',3'-bis-deoxy-5-fluorocytidine)
IT **147058-39-7**, β -L-2',3'-Dideoxy-5-fluorocytidine
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); USES (Uses)
(inhibition of the replication of **hepatitis B** virus in vitro
by β -L-2',3'-bis-deoxy-5-fluorocytidine)
RN **147058-39-7** HCAPLUS
CN **2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-
(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)**

Absolute stereochemistry. Rotation (-).



L34 ANSWER 39 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:293319 HCAPLUS
DOCUMENT NUMBER: 129:579
TITLE: Induction of **viral** mutation by incorporation
of miscoding ribonucleoside analogs into **viral**
RNA
INVENTOR(S): Loeb, Lawrence A.; Mullins, James I.
PATENT ASSIGNEE(S): University of Washington, USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9818324	A1	19980507	WO 1997-US19670	19971027
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
CA 2269213	AA	19980507	CA 1997-2269213	19971027
AU 9850959	A1	19980522	AU 1998-50959	19971027
AU 740916	B2	20011115		
EP 948256	A1	19991013	EP 1997-913882	19971027

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO

NZ 335000	A	20001222	NZ 1997-335000	19971027
JP 2001525797	T2	20011211	JP 1998-520739	19971027
NZ 507848	A	20050128	NZ 1997-507848	19971027

PRIORITY APPLN. INFO.:	US 1996-29404P	P	19961028
	US 1997-40535P	P	19970227
	WO 1997-US19670	W	19971027

AB The invention is directed to the identification and use of ribonucleoside analogs to induce the mutation of an RNA virus, including HIV and **HCV**, or a virus which otherwise replicates through an RNA intermediate. The increase in the mutation rate of the virus results in reduced viability of progeny generations of the virus, thereby inhibiting viral replication. In addition to these methods and related compns., the invention provides methods and combinatorial chemical libraries for screening ribonucleoside analogs for mutagenic potential.

IC ICM A01N043-04

ICS A61K031-70; C12N007-04; C12N007-06; C12Q001-68; C12Q001-70

CC 1-5 (Pharmacology)

Section cross-reference(s): 63

ST ribonucleoside analog virus mutation **antiviral**; screening **antiviral** ribonucleoside analog virus mutation; combinatorial library **antiviral** ribonucleoside analog

IT **Hepatitis**

(B; induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and screening method)

IT **Hepatitis**

(C; induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and screening method)

IT Antitumor agents

Antitumor agents

(T-cell leukemia; induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and screening method)

IT mRNA

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(analog; induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and screening method)

IT Animal tissue culture

Anti-AIDS agents

Antiviral agents

Combinatorial library

Coronavirus

Dengue virus

Drug delivery systems

Drug screening

Feline immunodeficiency virus

Feline leukemia virus

Hepatitis A virus

Hepatitis B virus

Hepatitis C virus

Human T-lymphotropic virus 1

Human T-lymphotropic virus 2

Human immunodeficiency virus

Human immunodeficiency virus 1

Human immunodeficiency virus 2

Influenza virus

Mutation
RNA viruses
Respiratory syncytial virus
Retroviridae
Simian immunodeficiency virus
Vesicular stomatitis virus
 (induction of **viral** mutation by incorporation of miscoding
 ribonucleoside analogs into **viral** RNA, and screening method)

IT Nucleoside analogs
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
 (induction of **viral** mutation by incorporation of miscoding
 ribonucleoside analogs into **viral** RNA, and screening method)

IT DNA
RNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
 (induction of **viral** mutation by incorporation of miscoding
 ribonucleoside analogs into **viral** RNA, and screening method)

IT Mutagens
 (mutagenic potential; induction of **viral** mutation by
 incorporation of miscoding ribonucleoside analogs into **viral**
 RNA, and screening method)

IT Virus
 (mutation rate; induction of **viral** mutation by incorporation
 of miscoding ribonucleoside analogs into **viral** RNA, and
 screening method)

IT Drug delivery systems
 (oral; induction of **viral** mutation by incorporation of
 miscoding ribonucleoside analogs into **viral** RNA, and
 screening method)

IT Drug delivery systems
 (parenterals; induction of **viral** mutation by incorporation of
 miscoding ribonucleoside analogs into **viral** RNA, and
 screening method)

IT Reactive oxygen species
RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction; induction of **viral** mutation by incorporation of
 miscoding ribonucleoside analogs into **viral** RNA, and
 screening method)

IT Nucleic acids
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
 (templates; induction of **viral** mutation by incorporation of
 miscoding ribonucleoside analogs into **viral** RNA, and
 screening method)

IT 65-46-3, Cytidine 66-22-8, Uracil, biological studies 73-24-5,
Adenine, biological studies 73-40-5, Guanine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
 (RNA nucleoside analog replacement of; induction of **viral**
 mutation by incorporation of miscoding ribonucleoside analogs into
 viral RNA, and screening method)

IT 9014-24-8, RNA polymerase
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
 (and RNA polymerase II; induction of **viral** mutation by
 incorporation of miscoding ribonucleoside analogs into **viral**

RNA, and screening method)

IT 58-61-7D, Adenosine, derivs., biological studies 58-96-8D, Uridine, derivs. 65-46-3D, Cytidine, derivs. 118-00-3D, Guanosine, derivs., biological studies 957-77-7, 5-Hydroxyuridine 957-77-7D, 5-Hydroxyuridine, derivs. 1867-73-8 1867-73-8D, derivs. 2140-64-9, 3-Methylcytidine 2140-64-9D, 3-Methylcytidine, derivs. 2140-69-4, 3-Methyluridine 2140-69-4D, 3-Methyluridine, derivs. 2149-76-0, 5-Aminouridine 2149-76-0D, 5-Aminouridine, derivs. **3066-86-2**, 5-Bromocytidine **3066-86-2D**, 5-Bromocytidine, derivs. 3868-31-3, 8-Hydroxyguanosine 3868-31-3D, 8-Hydroxyguanosine, derivs. 3868-32-4, 8-Aminoguanosine 3868-32-4D, 8-Aminoguanosine, derivs. 7803-88-5 7803-88-5D, derivs. 13007-43-7 13007-43-7D, derivs. 23899-77-6, 5-Aminocytidine 23899-77-6D, 5-Aminocytidine, derivs. **25130-29-4**, 5-Chlorocytidine **25130-29-4D**, 5-Chlorocytidine, derivs. 33962-59-3 33962-59-3D, derivs. 34218-77-4 34218-77-4D, derivs. 39007-51-7 39007-51-7D, derivs. 39007-52-8 39007-52-8D, derivs. 39638-73-8 39638-73-8D, derivs. 39708-01-5 39708-01-5D, derivs. 53337-88-5 53337-88-5D, derivs. 53337-89-6 53337-89-6D, derivs. 57294-74-3 57294-74-3D, derivs. 59495-20-4 59495-20-4D, derivs. 72055-62-0, 3-Methyladenosine 72055-62-0D, 3-Methyladenosine, derivs. 82773-20-4 82773-20-4D, derivs. 100997-68-0 100997-68-0D, derivs. 108060-85-1 108060-85-1D, derivs. 137248-64-7 137248-64-7D, derivs. 207340-54-3 207340-54-3D, derivs. 207340-56-5 207340-56-5D, derivs. 207340-58-7 207340-58-7D, derivs.

RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and screening method)

IT 65-71-4, Thymine 71-30-7, Cytosine

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and screening method)

IT 7782-44-7D, Oxygen, free radicals, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction; induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and screening method)

IT **3066-86-2**, 5-Bromocytidine **3066-86-2D**, 5-Bromocytidine, derivs. **25130-29-4**, 5-Chlorocytidine **25130-29-4D**, 5-Chlorocytidine, derivs.

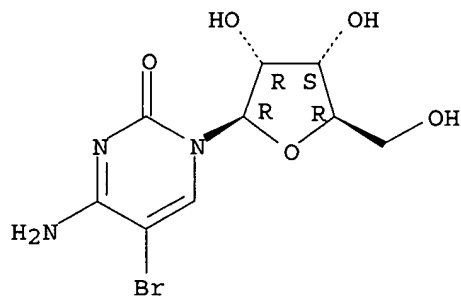
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(induction of **viral** mutation by incorporation of miscoding ribonucleoside analogs into **viral** RNA, and screening method)

RN 3066-86-2 HCAPLUS

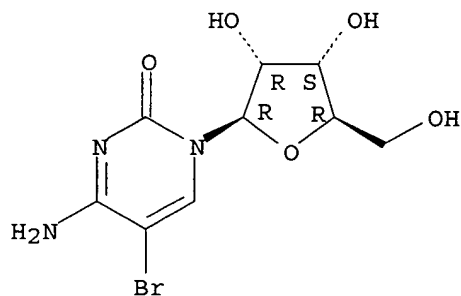
CN Cytidine, 5-bromo- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



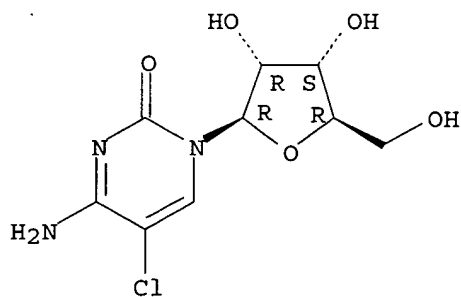
RN 3066-86-2 HCAPLUS
CN Cytidine, 5-bromo- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



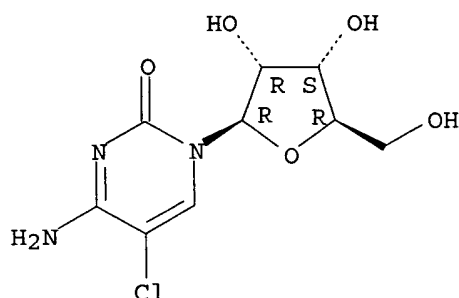
RN 25130-29-4 HCAPLUS
CN Cytidine, 5-chloro- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 25130-29-4 HCAPLUS
CN Cytidine, 5-chloro- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 40 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:268360 HCAPLUS

DOCUMENT NUMBER: 128:308706

TITLE: Preparation of monophosphate prodrugs of β -L-FD4C and β -L-FddC as potent **antiviral** agents

INVENTOR(S): Li, Xiuyan; Chen, Shu-hui; Carmichael, Ellen; Doyle, Terrence W.; Cheng, Yung-chi

PATENT ASSIGNEE(S): Vion Pharmaceuticals, Inc., USA; Yale University

SOURCE: PCT Int. Appl., 53 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9817281	A1	19980430	WO 1997-US18860	19971023
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9749886	A1	19980515	AU 1997-49886	19971023
PRIORITY APPLN. INFO.:			US 1996-736156	A2 19961024
			WO 1997-US18860	W 19971023

OTHER SOURCE(S): MARPAT 128:308706

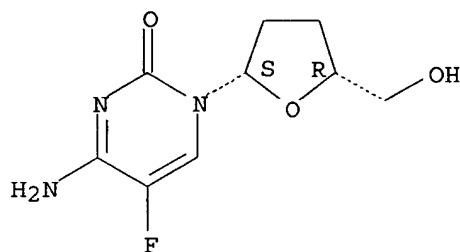
AB The present invention relates to certain prodrug forms of the L-dideoxynucleoside analogs β -L-FD4C and β -L-FddC, especially β -L-FD4C, which preferably contain S-acyl-2-thioethyl-bearing 5'-monophosphate groups which exhibit excellent activity against **hepatitis B virus (HBV)** and human immunodeficiency virus (HIV). In particular, the compds. according to the present invention show potent inhibition of the replication of the virus in combination with very low toxicity to the host cells (i.e, animal or human tissue) and unexpectedly high therapeutic indexes. The prodrug form of β -L-FD4C exhibits particularly effective inhibition of HBV in comparison to β -L-FD4C and markedly improved therapeutic index.

IC ICM A61K031-70

ICS C07H019-10; C07H019-20

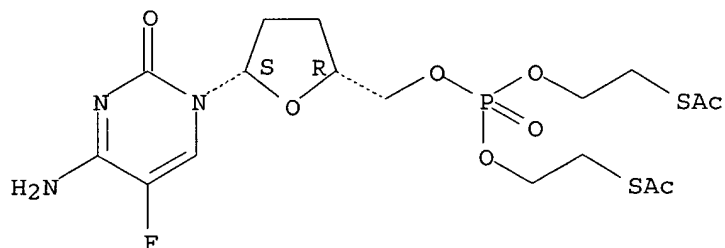
- CC 33-9 (Carbohydrates)
Section cross-reference(s): 1, 63
- ST **hepatitis B virus antiviral** dideoxynucleoside prepn;
dideoxynucleoside prepn **antiviral** AIDS treatment
- IT Nucleosides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dideoxy; preparation of monophosphate prodrugs of β -L-FD4C and β -L-FddC as potent **antiviral** agents)
- IT AIDS (disease)
Antiviral agents
Cytotoxicity
Hepatitis B virus
T cell (lymphocyte)
(preparation of monophosphate prodrugs of β -L-FD4C and β -L-FddC as potent **antiviral** agents)
- IT 147058-39-7P 181785-84-2P 203635-05-6P 206351-25-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of monophosphate prodrugs of β -L-FD4C and β -L-FddC as potent **antiviral** agents)
- IT 90-01-7 623-05-2 6893-26-1, D-Glutamic acid 15097-49-1,
N-(Trimethylsilyl) pyrrolidine 41858-09-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of monophosphate prodrugs of β -L-FD4C and β -L-FddC as potent **antiviral** agents)
- IT 5666-12-6P 33019-03-3P 52813-63-5P 53558-93-3P 59012-91-8P
69128-17-2P 113068-75-0P 128075-94-5P 168777-53-5P 189818-62-0P
189818-63-1P 189818-64-2P 189818-65-3P 189818-66-4P 189818-67-5P
203635-01-2P 203635-02-3P 203635-04-5P 206351-26-0P 206351-27-1P
206351-28-2P 206351-29-3P 206351-31-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of monophosphate prodrugs of β -L-FD4C and β -L-FddC as potent **antiviral** agents)
- IT 206351-30-6P 206351-32-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of monophosphate prodrugs of β -L-FD4C and β -L-FddC as potent **antiviral** agents)
- IT 147058-39-7P 206351-25-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of monophosphate prodrugs of β -L-FD4C and β -L-FddC as potent **antiviral** agents)
- RN 147058-39-7 HCAPLUS
- CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 206351-25-9 HCAPLUS
CN Ethanethioic acid, S,S'-[[[(2R,5S)-5-(4-amino-5-fluoro-2-oxo-1(2H)-pyrimidinyl)tetrahydro-2-furanyl]methoxy]phosphinyldene]bis(oxy-2,1-ethanediyl)] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 41 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:638461 HCAPLUS

DOCUMENT NUMBER: 127:302913

TITLE: Structure-Activity Relationships of
2'-Deoxy-2',2'-difluoro-L-erythro-pentofuranosyl
Nucleosides

AUTHOR(S): Kotra, Lakshmi P.; Xiang, Yuejun; Newton, M. Gary;
Schinazi, Raymond F.; Cheng, Yung-C.; Chu, Chung K.

CORPORATE SOURCE: Department of Medicinal Chemistry College of Pharmacy
and Department of Chemistry, University of Georgia,
Athens, GA, 30602-2352, USA

SOURCE: Journal of Medicinal Chemistry (1997), 40(22),
3635-3644

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Following the recent discoveries that some L-nucleosides are more or equal potent than their D-counterparts, we synthesized 2'-deoxy-2',2'-difluoro-L-erythro-pentofuranosyl nucleosides as potential **antiviral** agents. The target compds. were synthesized via the key intermediates 7a or 7b from L-gulono γ -lactone. Compound 2 was oxidatively cleaved and coupled with Et bromodifluoroacetate in the presence of activated zinc under Reformatsky conditions to obtain a diastereomeric mixture of 4(R) and 4(S), in a 4:1 ratio. The major 4(R) isomer was cyclized and treated appropriately to obtain the mesylate 8a or 8b, which was condensed with various silyl-protected pyrimidines. Condensation of the alc. 7a or 7b

with 6-chloropurine under Mitsunobu conditions afforded the 6-chloropurine analogs 53a or 53b and 54a or 54b. Further treatment of the compds. 53a, 54a and 53b, 54b afforded the inosine and adenine derivs. 57-60, resp. The condensation of 2-amino-6-chloropurine with compound 8a and subsequent treatment with 2-mercaptoethanol/sodium methoxide afforded the guanine analogs 63 and 64. All of the synthesized nucleosides 31-52, 57-60, 63, and 64 were evaluated for **antiviral** activity and for cellular toxicity. Adenine derivative 57 showed a moderate activity against HIV-1 in PBM cells (3.4 μ M). None of the other compds. showed any significant activities against HIV-1, HBV, HSV-1, HSV-2, and toxicity in Vero, CEM, and PBM cell lines up to 100 μ M. The X-ray structure of the 5-iodocytosine analog showed a 2'-exo/3'-endo conformation for the carbohydrate moiety, which is different from those of the biol. active compds. (-)-FTC and L-FMAU.

CC 1-3 (Pharmacology)

ST **antiviral** deoxydifluoroerythro pentofuranosyl nucleoside prepn

IT Structure-activity relationship

(**antiviral**; preparation and structure-activity relationships of **antiviral** nucleosides)

IT **Antiviral** agents

Hepatitis B virus

Human herpesvirus 1

Human herpesvirus 2

Human immunodeficiency virus 1

(preparation and structure-activity relationships of **antiviral** nucleosides)

IT 166275-39-4P 166275-40-7P 197452-39-4P 197452-40-7P 197452-41-8P

197452-42-9P 197452-43-0P 197452-44-1P 197452-45-2P

197452-46-3P 197452-47-4P 197452-48-5P

197452-49-6P 197452-50-9P 197452-51-0P 197452-52-1P

197452-53-2P 197452-54-3P 197452-55-4P 197452-56-5P

197452-57-6P 197452-58-7P 197452-59-8P

197452-60-1P 197452-64-5P 197452-65-6P

RL: **BAC (Biological activity or effector, except adverse)**; BSU

(Biological study, unclassified); PRP (Properties); SPN (Synthetic

preparation); **THU (Therapeutic use)**; BIOL (Biological study);

PREP (Preparation); USES (Uses)

(preparation and structure-activity relationships of **antiviral** nucleosides)

IT 197452-68-9P 197452-69-0P

RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT

(Reactant or reagent); USES (Uses)

(preparation and structure-activity relationships of **antiviral** nucleosides)

IT 87-42-3, 6-Chloropurine 1128-23-0 72101-44-1

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation and structure-activity relationships of **antiviral** nucleosides)

IT 22323-80-4P 94697-68-4P 166275-25-8P 166275-26-9P 166275-27-0P

166275-29-2P 166275-31-6P 166275-37-2P 166275-38-3P 166376-97-2P

166376-98-3P 166376-99-4P 166377-00-0P 197452-15-6P 197452-16-7P

197452-17-8P 197452-18-9P 197452-19-0P 197452-20-3P 197452-21-4P

197452-22-5P 197452-23-6P 197452-24-7P 197452-25-8P 197452-26-9P

197452-27-0P 197452-28-1P 197452-29-2P 197452-30-5P 197452-31-6P

197452-32-7P 197452-33-8P 197452-34-9P 197452-35-0P 197452-36-1P

197452-37-2P 197452-38-3P 197452-61-2P 197452-62-3P 197452-66-7P

197452-67-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)

(preparation and structure-activity relationships of **antiviral** nucleosides)

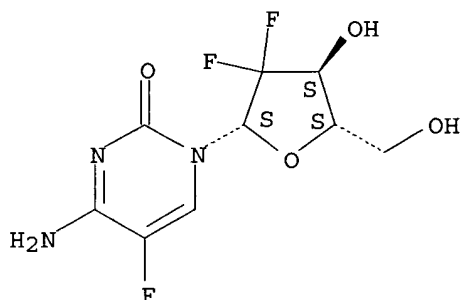
IT 197452-46-3P 197452-47-4P 197452-48-5P
197452-49-6P 197452-57-6P 197452-58-7P
197452-59-8P 197452-60-1P

RL: BAC (**Biological activity or effector, except adverse**); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (**Therapeutic use**); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and structure-activity relationships of **antiviral** nucleosides)

RN 197452-46-3 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy-2,2-difluoro-β-L-erythro-pentofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

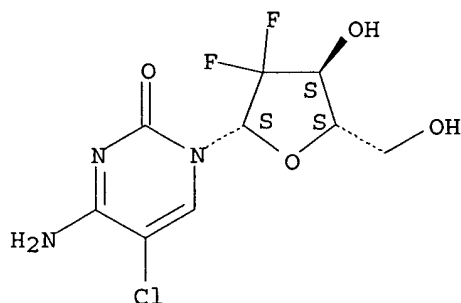
Absolute stereochemistry. Rotation (-).



RN 197452-47-4 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-chloro-1-(2-deoxy-2,2-difluoro-β-L-erythro-pentofuranosyl)- (9CI) (CA INDEX NAME)

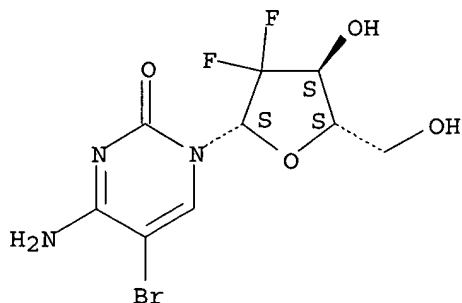
Absolute stereochemistry. Rotation (-).



RN 197452-48-5 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-bromo-1-(2-deoxy-2,2-difluoro-β-L-erythro-pentofuranosyl)- (9CI) (CA INDEX NAME)

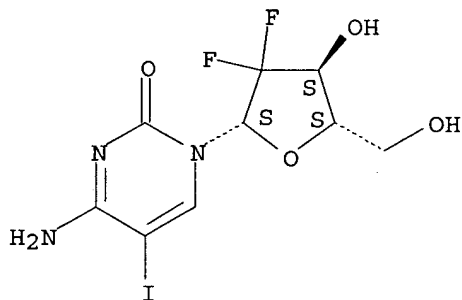
Absolute stereochemistry. Rotation (-).



RN 197452-49-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy-2,2-difluoro-β-L-erythro-pentofuranosyl)-5-iodo- (9CI) (CA INDEX NAME)

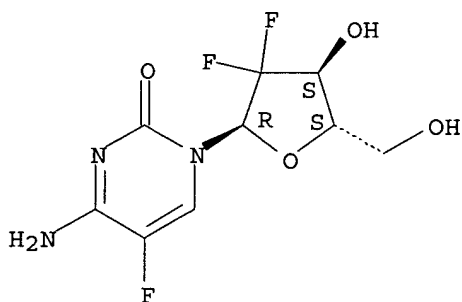
Absolute stereochemistry. Rotation (-).



RN 197452-57-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy-2,2-difluoro-α-L-erythro-pentofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

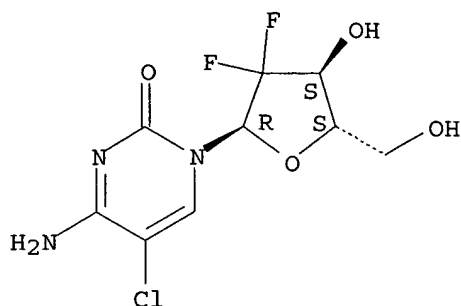
Absolute stereochemistry. Rotation (+).



RN 197452-58-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-chloro-1-(2-deoxy-2,2-difluoro-α-L-erythro-pentofuranosyl)- (9CI) (CA INDEX NAME)

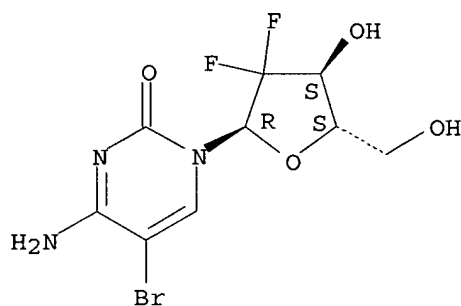
Absolute stereochemistry. Rotation (-).



RN 197452-59-8 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-bromo-1-(2-deoxy-2,2-difluoro-α-L-erythro-pentofuranosyl)- (9CI) (CA INDEX NAME)

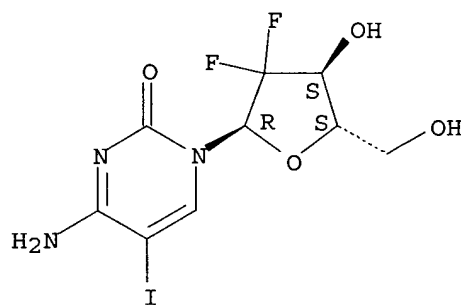
Absolute stereochemistry. Rotation (-).



RN 197452-60-1 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy-2,2-difluoro-α-L-erythro-pentofuranosyl)-5-iodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 42 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:344802 HCAPLUS

DOCUMENT NUMBER: 126:343812

TITLE: Preparation of L-2',3'-dideoxy nucleoside analogs as anti-hepatitis B (HBV) and anti-HIV agents

INVENTOR(S): Lin, Tai-shun; Cheng, Yung-chi
 PATENT ASSIGNEE(S): Yale University, USA
 SOURCE: U.S., 29 pp., Cont.-in-part of U.S. Ser. No. 67,299.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5627160	A	19970506	US 1993-98650	19930728
CA 2163520	AA	19941208	CA 1994-2163520	19940523
CA 2163520	C	20060110		
WO 9427616	A1	19941208	WO 1994-US5790	19940523
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9470430	A1	19941220	AU 1994-70430	19940523
AU 693795	B2	19980709		
EP 707481	A1	19960424	EP 1994-919207	19940523
EP 707481	B1	20000816		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08510747	T2	19961112	JP 1995-500872	19940523
AT 195423	E	20000915	AT 1994-919207	19940523
ES 2150993	T3	20001216	ES 1994-919207	19940523
PT 707481	T	20010228	PT 1994-919207	19940523
CN 1100303	A	19950322	CN 1994-106188	19940524
CN 1076021	B	20011212		
US 5561120	A	19961001	US 1995-456635	19950601
US 5631239	A	19970520	US 1995-544650	19951018
US 5830881	A	19981103	US 1996-724138	19960930
HK 1013257	A1	20010202	HK 1998-114607	19981222
GR 3034379	T3	20001229	GR 2000-402067	20000908
JP 2004244422	A2	20040902	JP 2004-106919	20040331
PRIORITY APPLN. INFO.:			US 1993-67299	A2 19930525
			US 1993-98650	A 19930728
			JP 1995-500872	A3 19940523
			WO 1994-US5790	W 19940523
			US 1995-456635	A3 19950601

OTHER SOURCE(S): MARPAT 126:343812

AB The present invention relates to the surprising discovery that certain dideoxynucleoside analogs which contain a dideoxy ribofuranosyl moiety having an L-configuration (as opposed to the naturally occurring D-configuration) exhibit unexpected activity against *hepatitis B* virus (HBV). In particular, the compds. according to the present invention show potent inhibition of the replication of the virus in combination with very low toxicity to the host cells (i.e., animal or human tissue). Compds. according to the present invention exhibit primary utility as agents for inhibiting the growth or replication of HBV, HIV and other retroviruses, most preferably HBV. The compound 1-(2,3-dideoxy-beta-L-ribofuranosyl)-5-fluorocytosine is shown to be a potent anti-HIV agent with low toxicity to host cells.

IC ICM A61K031-70

ICS C07H019-06

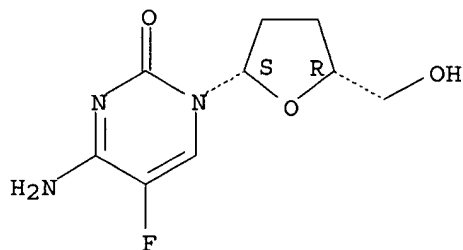
INCL 514049000

CC 33-9 (Carbohydrates)

Section cross-reference(s): 1, 63

- ST AIDS dideoxy nucleoside analog prepn; **hepatitis** B virucide
nucleoside analog prepn; dideoxy nucleoside analog prepn virucide
- IT **Antiviral agents**
(preparation of L-2',3'-dideoxy nucleoside analogs as anti-**hepatitis**
B and anti-HIV agents)
- IT AIDS (disease)
(treatment; preparation of L-2',3'-dideoxy nucleoside analogs as anti-
hepatitis B and anti-HIV agents)
- IT Nucleosides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(L-2',3'-dideoxy; preparation of L-2',3'-dideoxy nucleoside analogs as anti-
hepatitis B and anti-HIV agents)
- IT 7481-89-2P **147058-39-7P** 158850-60-3P 160963-03-1P
173398-50-0P
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); SPN (Synthetic preparation); **THU**
(**Therapeutic use**); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(preparation of L-2',3'-dideoxy nucleoside analogs as anti-**hepatitis**
B and anti-HIV agents)
- IT 51-20-7, 5-Bromouracil 51-21-8, 5-Fluorouracil 66-22-8, Uracil,
reactions 696-07-1, 5-Iodouracil 1820-81-1, 5-Chlorouracil
6893-26-1, D-Glutamic acid 31501-19-6 31501-46-9 153506-51-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of L-2',3'-dideoxy nucleoside analogs as anti-**hepatitis**
B and anti-HIV agents)
- IT 153506-49-1P 153506-50-4P 157084-97-4P 160963-02-0P 160963-04-2P
189998-52-5P 189998-53-6P 189998-56-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of L-2',3'-dideoxy nucleoside analogs as anti-**hepatitis**
B and anti-HIV agents)
- IT 121154-51-6P 135212-57-6P 153547-98-9P 153547-99-0P 160963-05-3P
160963-07-5P 160963-09-7P 160963-12-2P 164200-64-0P 189998-54-7P
189998-55-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of L-2',3'-dideoxy nucleoside analogs as anti-**hepatitis**
B and anti-HIV agents)
- IT **147058-39-7P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); SPN (Synthetic preparation); **THU**
(**Therapeutic use**); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(preparation of L-2',3'-dideoxy nucleoside analogs as anti-**hepatitis**
B and anti-HIV agents)
- RN 147058-39-7 HCAPLUS
- CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-
(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L34 ANSWER 43 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:145208 HCAPLUS

DOCUMENT NUMBER: 126:139863

TITLE: Stabilized nucleotides from nucleosides with anti-**hepatitis** B virus activity, nucleosides and nucleotides for treatment of **hepatitis** B virus infection, and compound preparation

INVENTOR(S): Schinazi, Raymond F.; Sommadossi, Jean-Pierre; Grosselin, Gilles; Imbach, Jean-Louis

PATENT ASSIGNEE(S): Emory University, USA; Uab Research Foundation; Centre National de la Recherche Scientifique

SOURCE: PCT Int. Appl., 51 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

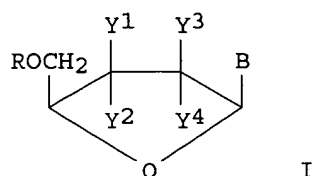
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640164	A1	19961219	WO 1996-US10026	19960607
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2219132	AA	19961219	CA 1996-2219132	19960607
CA 2538205	AA	19961219	CA 1996-2538205	19960607
AU 9661707	A1	19961230	AU 1996-61707	19960607
AU 722214	B2	20000727		
EP 831852	A1	19980401	EP 1996-919349	19960607
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11507381	T2	19990629	JP 1996-502163	19960607
EP 1655033	A1	20060510	EP 2005-77806	19960607
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6245749	B1	20010612	US 1998-112878	19980709
US 2002107221	A1	20020808	US 2001-879854	20010612
US 2005277616	A1	20051215	US 2005-180964	20050712
PRIORITY APPLN. INFO.:				
			US 1995-485716	A 19950607
			US 1994-320461	B2 19941007
			CA 1996-2219132	A3 19960607
			EP 1996-919349	A3 19960607
			WO 1996-US10026	W 19960607
			US 1998-112878	A1 19980709
			US 2001-879854	A1 20010612

OTHER SOURCE(S): MARPAT 126:139863
GI



- AB A method for the treatment of a host, in particular a human, infected with HBV is provided that includes administering an HBV-treatment amount of the stabilized nucleotide of a nucleoside which exhibits anti-**hepatitis B** activity. The nucleotides of the invention include I [B = purine base, pyrimidine base; Y1-Y4 = H, OH, N3, NO2, SH, halo, alkoxy, aryloxy, etc. (typically, 3 of Y1-Y4 are H or OH); R = stabilized phosphate derivative]. Preparation of e.g. β -L-2',3'-dideoxyadenosin-5'-yl bis(2-pivaloylthioethyl)phosphate is described.
- IC ICM A61K031-70
ICS C07H019-073; C07H019-10; C07H019-173; C07H019-20
- CC 1-5 (Pharmacology)
Section cross-reference(s): 33, 63
- ST stabilized nucleotide **hepatitis B antiviral**;
nucleoside nucleotide **antiviral hepatitis B**
- IT Drug delivery systems
(prodrugs; stabilized nucleotides from nucleosides with anti-**hepatitis B** virus activity, nucleosides and nucleotides for treatment of **hepatitis B** virus infection, and compound preparation)
- IT **Antiviral agents**
Drug delivery systems
Hepatitis B virus
(stabilized nucleotides from nucleosides with anti-**hepatitis B** virus activity, nucleosides and nucleotides for treatment of **hepatitis B** virus infection, and compound preparation)
- IT Nucleosides, biological studies
Nucleotides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(stabilized nucleotides from nucleosides with anti-**hepatitis B** virus activity, nucleosides and nucleotides for treatment of **hepatitis B** virus infection, and compound preparation)
- IT 186648-59-9P 186648-61-3P 186648-62-4P 186648-63-5P 186648-64-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction; stabilized nucleotides from nucleosides with anti-**hepatitis B** virus activity, nucleosides and nucleotides for treatment of **hepatitis B** virus infection, and compound preparation)
- IT 824-94-2, 4-Methoxybenzyl chloride 1972-28-7, Diethyl azodicarboxylate 169823-53-4 186648-58-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; stabilized nucleotides from nucleosides with anti-**hepatitis B** virus activity, nucleosides and nucleotides for treatment of **hepatitis B** virus infection, and compound preparation)
- IT 121154-51-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

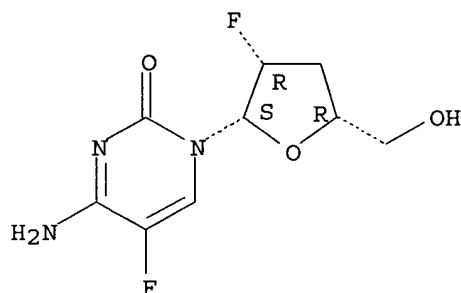
- (stabilized nucleotides from nucleosides with anti-**hepatitis** B virus activity, nucleosides and nucleotides for treatment of **hepatitis** B virus infection, and compound preparation)
- IT 61246-68-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(stabilized nucleotides from nucleosides with anti-**hepatitis** B virus activity, nucleosides and nucleotides for treatment of **hepatitis** B virus infection, and compound preparation)
- IT 132979-39-6P 186648-57-7P **186648-60-2P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(stabilized nucleotides from nucleosides with anti-**hepatitis** B virus activity, nucleosides and nucleotides for treatment of **hepatitis** B virus infection, and compound preparation)
- IT 144177-27-5 144490-04-0 **161170-31-6** 186648-65-7
186648-66-8
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(stabilized nucleotides from nucleosides with anti-**hepatitis** B virus activity, nucleosides and nucleotides for treatment of **hepatitis** B virus infection, and compound preparation)
- IT **147058-39-7D**, β -L-2',3'-Dideoxy-5-fluorocytidine, nucleotide derivs.
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(stabilized prodrugs; stabilized nucleotides from nucleosides with anti-**hepatitis** B virus activity, nucleosides and nucleotides for treatment of **hepatitis** B virus infection, and compound preparation)
- IT 137530-41-7D, nucleotide derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stabilized prodrugs; stabilized nucleotides from nucleosides with anti-**hepatitis** B virus activity, nucleosides and nucleotides for treatment of **hepatitis** B virus infection, and compound preparation)
- IT 3056-17-5D, D4T, nucleotide derivs. 7481-89-2D, 2',3'-Dideoxycytidine, nucleotide derivs. 30516-87-1D, AZT, nucleotide derivs. 69655-05-6D, DDI, nucleotide derivs. 134678-17-4D, nucleotide derivs. 143491-54-7D, nucleotide derivs. 143491-57-0D, (-)- β -L-2-Hydroxymethyl-5-(5-fluorocytosin-1-yl)-1,3-oxathiolane, nucleotide derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stabilized prodrugs; stabilized nucleotides from nucleosides with anti-**hepatitis** B virus activity, nucleosides and nucleotides for treatment of **hepatitis** B virus infection, and compound preparation)
- IT **186648-60-2P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(stabilized nucleotides from nucleosides with anti-**hepatitis**

B virus activity, nucleosides and nucleotides for treatment of
hepatitis B virus infection, and compound preparation)

RN 186648-60-2 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2,3-dideoxy-2-fluoro-β-L-threo-
pentofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 161170-31-6

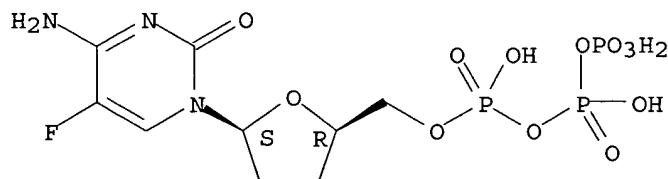
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); USES (Uses)

(stabilized nucleotides from nucleosides with anti-**hepatitis**
B virus activity, nucleosides and nucleotides for treatment of
hepatitis B virus infection, and compound preparation)

RN 161170-31-6 HCAPLUS

CN Triphosphoric acid, P-[(2R,5S)-[5-(4-amino-5-fluoro-2-oxo-1(2H)-
pyrimidinyl)tetrahydro-2-furanyl]methyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 147058-39-7D, β-L-2',3'-Dideoxy-5-fluorocytidine, nucleotide
derivs.

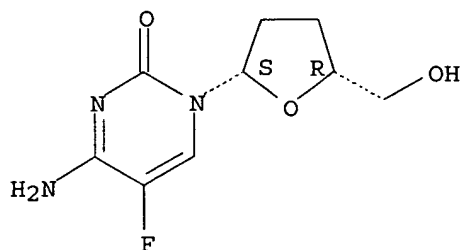
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); PRP (Properties); **THU (Therapeutic**
use); BIOL (Biological study); USES (Uses)

(stabilized prodrugs; stabilized nucleotides from nucleosides with
anti-**hepatitis** B virus activity, nucleosides and nucleotides
for treatment of **hepatitis** B virus infection, and compound
preparation)

RN 147058-39-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-
(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L34 ANSWER 44 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:596020 HCAPLUS

DOCUMENT NUMBER: 125:265990

TITLE: (5-Carboxamido or 5-fluoro)-(2',3'-unsaturated or 3'-modified)-pyrimidine nucleosides, preparation, and compositions and use for treatment of HIV and HBV infections

INVENTOR(S): Schinazi, Raymond F.; Liotta, Dennis C.

PATENT ASSIGNEE(S): Emory University, USA

SOURCE: PCT Int. Appl., 44 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9622778	A1	19960801	WO 1996-US965	19960129
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5703058	A	19971230	US 1995-379276	19950127
CA 2211612	AA	19960801	CA 1996-2211612	19960129
CA 2211612	C	20060815		
CA 2546745	AA	19960801	CA 1996-2546745	19960129
AU 9647056	A1	19960814	AU 1996-47056	19960129
AU 717580	B2	20000330		
EP 805683	A1	19971112	EP 1996-902772	19960129
EP 805683	B1	20051228		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 10512887	T2	19981208	JP 1996-522990	19960129
EP 1361227	A2	20031112	EP 2003-76825	19960129
EP 1361227	A3	20040303		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
AT 314077	E	20060115	AT 1996-902772	19960129
ES 2255710	T3	20060701	ES 1996-902772	19960129
US 5905070	A	19990518	US 1997-1084	19971230
US 6232300	B1	20010515	US 1999-310823	19990512
US 6391859	B1	20020521	US 2000-677161	20001002
US 2002198173	A1	20021226	US 2002-146779	20020515
US 6680303	B2	20040120		
US 2004167140	A1	20040826	US 2004-759985	20040116
JP 2005325128	A2	20051124	JP 2005-174655	20050615
PRIORITY APPLN. INFO.:			US 1995-379276	A 19950127
			CA 1996-2211612	A3 19960129
			EP 1996-902772	A3 19960129
			JP 1996-522990	A3 19960129

WO 1996-US965	W 19960129
US 1997-310823	A1 19970512
US 1997-1084	A1 19971230
US 1999-310823	A1 19990512
US 2000-677161	A1 20001002
US 2002-146779	A1 20020515

OTHER SOURCE(S): MARPAT 125:265990

AB A method and composition for the treatment of HIV an HBV infections in humans and other host animals is disclosed that includes the administration of an effective amount of a [5-carboxamido or 5-fluoro]-2',3'-didehydro-pyrimidine nucleoside or a [5-carboxamido or 5-fluoro]-3'-modified-pyrimidine nucleoside, mixts. thereof, or a pharmaceutically acceptable derivative or derivs. thereof, including an N-1 or N-4 alkylated or acylated derivative, or a pharmaceutically acceptable salt thereof, in a pharmaceutically acceptable carrier. Preparation and activity of compds. of the invention are included.

IC ICM A61K031-70

ICS A61K031-52; A61K031-505; C07H019-073; C07H019-10; C07D473-16; C07D473-34; C07D405-04; C07D473-00

CC 1-5 (Pharmacology)

Section cross-reference(s): 33, 63

ST pyrimidine nucleoside deriv prepn **antiviral**; HIV HBV

antiviral pyrimidine nucleoside deriv

IT Virus, animal

(**hepatitis B**, pyrimidine nucleoside derivative preparation, compns., and use for treatment of HIV and HBV infections)

IT 107036-62-4 134379-77-4 147058-39-7 153606-40-7

160707-70-0	160707-71-1	176485-54-4	181623-80-3	181623-84-7
181623-85-8	181623-86-9	181623-90-5	181623-92-7	181623-93-8
181623-94-9	181623-95-0	181623-96-1	181623-97-2	181623-98-3
181623-99-4	181624-00-0	181624-01-1	181624-02-2	181624-03-3
181624-04-4	181785-73-9	181785-74-0	181785-75-1	181785-76-2
181785-77-3	181785-78-4	181785-79-5	181785-80-8	181785-81-9
181785-82-0	181785-83-1	181785-84-2	181785-85-3	181785-86-4
181785-87-5	181785-88-6	181785-89-7	181785-90-0	
181785-91-1	181785-92-2	181785-93-3	181785-94-4	181785-95-5
181785-96-6	181785-97-7	181785-98-8	181785-99-9	181786-00-5
181786-01-6	181786-02-7	181786-03-8	181786-04-9	181786-05-0
181786-06-1	181786-07-2	181786-08-3	181786-09-4	

RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(pyrimidine nucleoside derivative preparation, compns., and use for treatment of

HIV and HBV infections)

IT 107036-62-4 147058-39-7 181785-87-5

RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

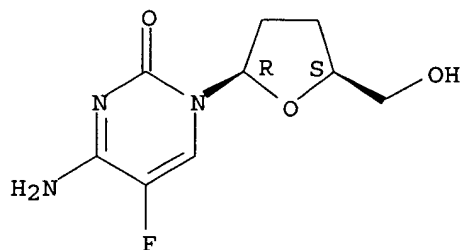
(pyrimidine nucleoside derivative preparation, compns., and use for treatment of

HIV and HBV infections)

RN 107036-62-4 HCAPLUS

CN Cytidine, 2',3'-dideoxy-5-fluoro- (9CI) (CA INDEX NAME)

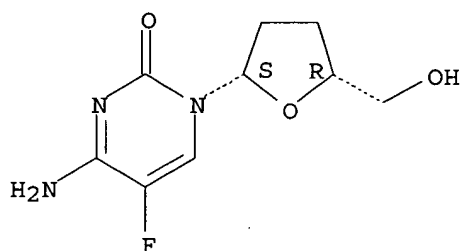
Absolute stereochemistry.



RN 147058-39-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

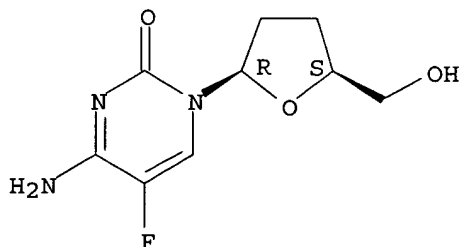
Absolute stereochemistry. Rotation (-).



RN 181785-87-5 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2R,5S)-tetrahydro-5-(hydroxymethyl)-2-furanyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L34 ANSWER 45 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:446493 HCAPLUS

DOCUMENT NUMBER: 125:115084

TITLE: Novel β -L-pyrimidine and β -L-purine nucleosides and their use as pharmaceutically active agents

INVENTOR(S): Matthes, Eckart; Von Janta-Lipinski, Martin

PATENT ASSIGNEE(S): Max-Delbrueck-Centrum Fuer Molekulare Medizin, Germany

SOURCE: PCT Int. Appl., 14 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9611204	A1	19960418	WO 1995-DE1412	19951005
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
PRIORITY APPLN. INFO.:			DE 1994-4436995	A 19941007
			DE 1995-19518261	A 19950510

OTHER SOURCE(S): MARPAT 125:115084

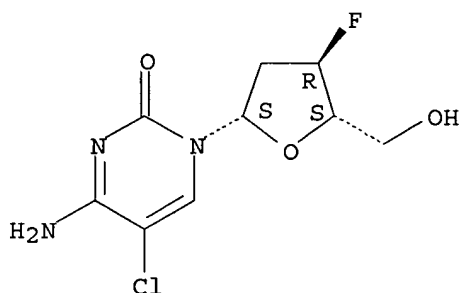
- AB Novel β -L-pyrimidine and β -L-purine nucleosides, such as β -L-2',3'-dideoxy-3'-fluorocytidine, β -L-2',3'-dideoxy-3'-fluoro-5-methylcytidine (I), β -L-2',3'-dideoxy-3'-fluoro-5-chlorocytidine, β -L-2',3'-dideoxy-3'-fluoroguanosine and β -L-5-methylcytosinearabinoside, and their use as pharmaceutically active substances and agents for the prophylaxis and/or treatment of infections caused by the **hepatitis-B** virus and the AIDS virus are described. Thus I, prepared by keeping 1-(5-O-acetyl-2,3-dideoxy-3-fluoro- β -L-ribofuranosyl)thymine, 1,2,4-triazole and 4-chlorophenyl dichlorophosphate in pyridine for 5 days, showed **antiviral** activity toward **hepatitis-B** virus.
- IC ICM C07H019-06
ICS C07H019-10; C07H019-20; C07H019-16; A61K031-70
- CC 33-9 (Carbohydrates)
Section cross-reference(s): 1
- ST pyrimidine purine nucleoside **antiviral** agent; HIV treatment
purine pyrimidine nucleoside; **hepatitis B** treatment purine
pyrimidine nucleoside; AIDS treatment purine pyrimidine nucleoside
- IT Nucleosides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of β -nucleosides as **antiviral** agents in treatment of AIDS and **hepatitis B** virus)
- IT Virus, animal
(**hepatitis B**, β -L-pyrimidine and β -L-purine nucleosides in treatment of)
- IT Virus, animal
(human immunodeficiency, preparation of β -nucleosides as **antiviral** agents in treatment of AIDS and **hepatitis B** virus)
- IT 177365-14-9P 178929-94-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of β -nucleosides as **antiviral** agents in treatment of AIDS and **hepatitis B** virus)
- IT 177365-12-7 177365-15-0 177365-16-1 177365-17-2
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(preparation of β -nucleosides as **antiviral** agents in treatment of AIDS and **hepatitis B** virus)
- IT 177365-13-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of β -nucleosides as **antiviral** agents in treatment of AIDS and **hepatitis B** virus)
- IT 177365-15-0
RL: **BAC (Biological activity or effector, except adverse)**; BSU

(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); USES (Uses)
(preparation of β -nucleosides as **antiviral** agents in
treatment of AIDS and **hepatitis B** virus)

RN 177365-15-0 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-chloro-1-(2,3-dideoxy-3-fluoro- β -L-
erythro-pentofuranosyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L34 ANSWER 46 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:354140 HCAPLUS

DOCUMENT NUMBER: 125:75333

TITLE: Structure-Activity Relationships of
1-(2-Deoxy-2-fluoro- β -L-arabino-
furanosyl)pyrimidine Nucleosides as Anti-
Hepatitis B Virus Agents

AUTHOR(S): Ma, Tianwei; Pai, S. Balakrishna; Zhu, Yong Lian; Lin,
Ju Sheng; Shanmuganathan, Kirupa; Du, Jinfa; Wang,
Chunguang; Kim, Hongbum; Newton, M. Gary; et al.

CORPORATE SOURCE: College of Pharmacy, University of Georgia, Athens,
GA, 30602, USA

SOURCE: Journal of Medicinal Chemistry (1996), 39(14),
2835-2843

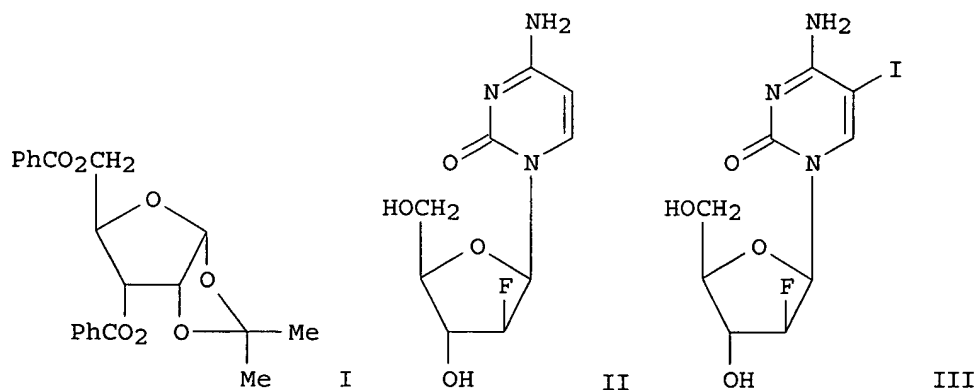
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



- AB Since 2'-fluoro-5-methyl- β -L-arabinofuranosyluracil (L-FMAU) has been shown to be a potent anti-HBV agent in vitro, it was of interest to study the structure-activity relationships of related nucleosides. Thus, a series of 1-(2-deoxy-2-fluoro- β -L-arabinofuranosyl)pyrimidine nucleosides have been synthesized and evaluated for **antiviral** activity against HBV in 2.2.15 cells. For this study, L-ribose was initially used as the starting material. Due to the com. cost of L-ribose, we have developed an efficient procedure for the preparation of L-ribose derivative I. Starting from L-xylose, I was obtained in an excellent total yield (70%) through the pyridinium dichromate oxidation of the 3-OH group followed by stereoselective reduction with NaBH₄. It was further converted to the 1,3,5-tri-O-benzoyl-2-deoxy-2-fluoro- α -L-arabinofuranose, which was then condensed with various 5-substituted pyrimidine bases to give the nucleosides. Among the compds. synthesized, the lead compound, L-FMAU, exhibited the most potent anti-HBV activity (EC₅₀ 0.1 μ M). None of the other uracil derivs. showed significant anti-HBV activity up to 10 μ M. Among the cytosine analogs, the cytosine (II) and 5-iodocytosine (III) derivs. showed moderately potent anti-HBV activity (EC₅₀ 1.4 and 5 μ M, resp.). The cytotoxicity of these nucleoside analogs has also been assessed in 2.2.15 cells as well as CEM cells. None of these compds. displayed any toxicity up to 200 μ M in 2.2.15 cells. Thus, L-FMAU, II, and III showed a selectivity of over 2000, 140, and 40, resp.
- CC 1-3 (Pharmacology)
Section cross-reference(s): 33
- ST arabinofuranosyl pyrimidine nucleoside **hepatitis** B virus;
structure activity arabinofuranosyl pyrimidine nucleoside virucide
- IT Molecular structure-biological activity relationship
Virucides and Virustats
(structure-activity relationships of 1-(2-deoxy-2-fluoro- β -L-arabino- furanosyl)pyrimidine nucleosides as anti-**hepatitis** B virus agents)
- IT Virus, animal
(**hepatitis** B, structure-activity relationships of 1-(2-deoxy-2-fluoro- β -L-arabino- furanosyl)pyrimidine nucleosides as anti-**hepatitis** B virus agents)
- IT 3080-30-6P 114861-22-2P 166411-39-8P 166411-40-1P 171720-99-3P
171721-00-9P 171721-03-2P 171721-04-3P 171721-05-4P 171721-06-5P
171721-11-2P 171721-12-3P 171866-29-8P 171866-30-1P 172949-42-7P
178687-86-0P 178687-87-1P 178687-89-3P 178687-91-7P 178687-93-9P
178687-95-1P 178687-97-3P 178687-99-5P 178688-03-4P 178688-04-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; structure-activity relationships of 1-(2-deoxy-2-fluoro- β -L-arabino- furanosyl)pyrimidine nucleosides as anti-**hepatitis** B virus agents)
- IT 54-20-6D, 5-(Trifluoromethyl)uracil, silylated 609-06-3, L-Xylose
696-07-1D, 5-Iodouracil, silylated 1066-54-2, (Trimethylsilyl)acetylene
2022-85-7D, 5-Fluorocytosine, silylated 2240-25-7D, 5-Bromocytosine, silylated 2347-43-5D, 5-Chlorocytosine, silylated 24259-59-4, L-Ribose
145913-85-5D, silylated
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; structure-activity relationships of 1-(2-deoxy-2-fluoro- β -L-arabino- furanosyl)pyrimidine nucleosides as anti-**hepatitis** B virus agents)
- IT 163252-36-6P **163686-34-8P** 163686-35-9P 171720-95-9P
171720-96-0P 178687-88-2P 178687-90-6P 178687-92-8P 178687-94-0P
178687-96-2P 178687-98-4P 178688-00-1P

178688-02-3P 178688-05-6P

RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)

(structure-activity relationships of 1-(2-deoxy-2-fluoro- β -L-arabino- furanosyl)pyrimidine nucleosides as anti-**hepatitis B** virus agents)

IT 178688-01-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(structure-activity relationships of 1-(2-deoxy-2-fluoro- β -L-arabino- furanosyl)pyrimidine nucleosides as anti-**hepatitis B** virus agents)

IT 163686-34-8P 178687-96-2P 178687-98-4P

178688-00-1P

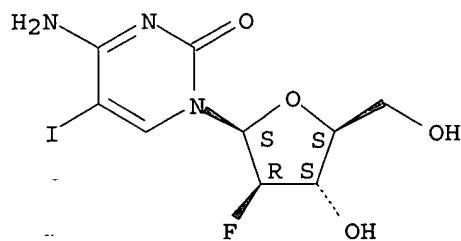
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)

(structure-activity relationships of 1-(2-deoxy-2-fluoro- β -L-arabino- furanosyl)pyrimidine nucleosides as anti-**hepatitis B** virus agents)

RN 163686-34-8 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy-2-fluoro- β -L-arabinofuranosyl)-5-iodo- (9CI) (CA INDEX NAME)

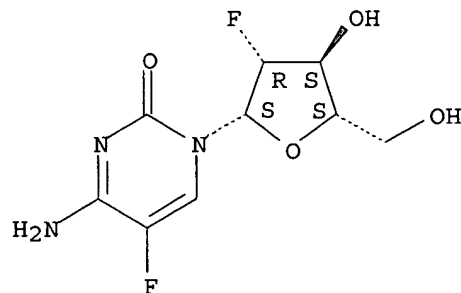
Absolute stereochemistry.



RN 178687-96-2 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy-2-fluoro- β -L-arabinofuranosyl)-5-fluoro- (9CI) (CA INDEX NAME)

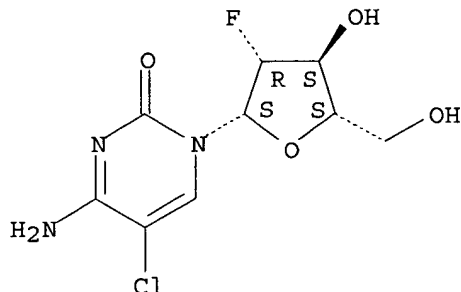
Absolute stereochemistry.



RN 178687-98-4 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-chloro-1-(2-deoxy-2-fluoro- β -L-arabinofuranosyl)- (9CI) (CA INDEX NAME)

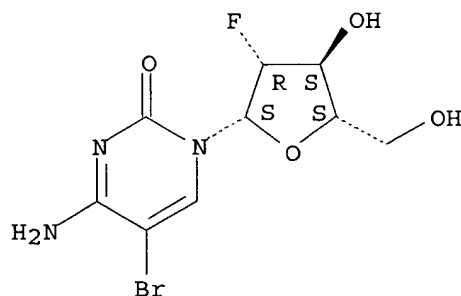
Absolute stereochemistry.



RN 178688-00-1 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-bromo-1-(2-deoxy-2-fluoro- β -L-arabinofuranosyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L34 ANSWER 47 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:202940 HCAPLUS

DOCUMENT NUMBER: 124:343946

TITLE: Design and Synthesis of 2',3'-Dideoxy-2',3'-didehydro- β -L-cytidine (β -L-d4C) and 2',3'-Dideoxy-2',3'-didehydro- β -L-5-fluorocytidine (β -L-Fd4C), Two Exceptionally Potent Inhibitors of Human *Hepatitis* B Virus (HBV) and Potent Inhibitors of Human Immunodeficiency Virus (HIV) in Vitro

AUTHOR(S): Lin, Tai-Shun; Luo, Mei-Zhen; Liu, Mao-Chin; Zhu, Yong-Lian; Gullen, Elizabeth; Dutschman, Ginger E.; Cheng, Yung-Chi

CORPORATE SOURCE: School of Medicine, Yale University, New Haven, CT, 06520-8066, USA

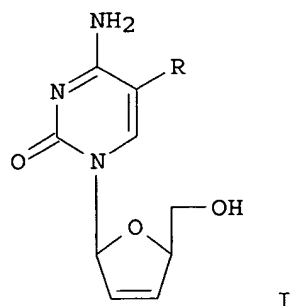
SOURCE: Journal of Medicinal Chemistry (1996), 39(9), 1757-9
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB Dideoxydidehydrocytidines I (R = H = F) have been synthesized and evaluated in vitro as potential anti-HBV and anti-HIV agents. The key intermediate 3',5'-dibenzoyl-2'-deoxy- β -L-uridin, which was synthesized from L-arabinose, was reacted with silylated 5-fluorouracil using trimethylsilyl trifluoromethanesulfonate as a catalyst to afford a mixture of the α and β anomers, 3',5'-dibenzoyl-2'-deoxy- α -L-5-fluorouridine and 3',5'-dibenzoyl-2'-deoxy- β -L-5-fluorouridine. I and II along with the known **antiviral** compds. β -D-ddC, β -D-d4C, β -L-FddC and β -L-SddC, were tested for their **antiviral** activities in vitro. Among these nucleoside analogs, II was found to be most active against HBV followed in decreasing activity by I; β -L-SddC; β -L-FddC. In addition, the compds. exhibiting activity against HIV in decreasing **antiviral** activity were: II; β -L-FddC; β -D-d4C; I; β -D-ddC; β -L-SddC. Since patients receiving long-term, anti-HBV or anti-HIV nucleoside therapy have experienced delayed toxicity, which may be linked to the drugs inhibition of mitochondrial DNA synthesis, the effect of I and II in decreasing the mitochondrial DNA content in cells upon long-term exposure to these two drugs was also studied. Both compds. showed no effect on mitochondrial DNA content of CEM cells after a 6 day exposure at 10 μ M, which is a much higher concentration required to inhibit HBV in culture. To the best of our knowledge, II appears to be the most potent and selective compound against HBV reported to date. Thus, these two compds. merit further development as potential anti-HBV and anti-HIV agents.

CC 33-9 (Carbohydrates)

Section cross-reference(s): 1

IT Virucides and Virustats

(synthesis and **antiviral** activity of dideoxydidehydrocytidines)

IT Toxicity

(cytotoxicity, synthesis and **antiviral** activity of dideoxydidehydrocytidines)

IT 7481-88-1 7481-89-2 136846-20-3 147058-41-1

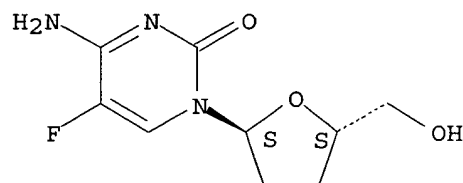
RL: BAC (**Biological activity or effector, except adverse**); BSU (Biological study, unclassified); BIOL (Biological study) (synthesis and **antiviral** activity of dideoxydidehydrocytidines)

IT 148766-47-6P 176485-54-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis and **antiviral** activity of
dideoxydidehydrocytidines)
IT 17242-85-2 31615-99-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and **antiviral** activity of
dideoxydidehydrocytidines)
IT 31501-19-6P 77180-78-0P 176247-02-2P 176247-03-3P 176247-04-4P
176247-05-5P 176247-06-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(synthesis and **antiviral** activity of
dideoxydidehydrocytidines)
IT 77180-98-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis and **antiviral** activity of
dideoxydidehydrocytidines)
IT 147058-41-1
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); BIOL (Biological study)
(synthesis and **antiviral** activity of
dideoxydidehydrocytidines)
RN 147058-41-1 HCAPLUS
CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[tetrahydro-5-(hydroxymethyl)-2-
furanyl]-, (2S-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L34 ANSWER 48 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:86176 HCAPLUS
DOCUMENT NUMBER: 124:193419
TITLE: 2',3'-Dideoxy-β-L-5-fluorocytidine inhibits duck
hepatitis B virus reverse transcription and
suppresses **viral** DNA synthesis in
hepatocytes, both in vitro and in vivo
AUTHOR(S): Zoulim, Fabien; Dannaoui, Eric; Borel, Christelle;
Hantz, Olivier; Lin, Tai-Shun; Liu, Shuey-Huey; Trepo,
Christian; Cheng, Yung-Chi
CORPORATE SOURCE: Inst. Natl. Sante Rech. Med., Lyon, 69003, Fr.
SOURCE: Antimicrobial Agents and Chemotherapy (1996), 40(2),
448-53
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB β-L-Nucleoside analogs represent a new class of potent
antiviral agents with low cytotoxicity which provide new hope in
the therapy of chronic **hepatitis B** virus (HBV) infections. The
authors evaluated the anti-HBV activity of 2',3'-dideoxy-β-L-5-
fluorocytidine (β-L-F-ddC), a β-L-nucleoside analog derived from

2',3'-dideoxycytidine (ddC), in the duck HBV (DHBV) model. This compound was previously shown to inhibit HBV DNA synthesis in a stably transfected hepatoma cell line (F2215). Using a cell-free system for the expression of an enzymically active DHBV polymerase, the authors could demonstrate that the triphosphate form of β -L-F-ddC does inhibit hepadnavirus reverse transcription. In primary duck hepatocyte culture, β -L-F-ddC showed a potent inhibitory effect on DHBV DNA synthesis which was concentration dependent. Although β -L-F-ddC was shown to be less active than ddC against the DHBV reverse transcriptase in vitro, β -L-F-ddC was a stronger inhibitor in hepatocytes. The oral administration of β -L-F-ddC in exptl. infected ducklings showed that β -L-F-ddC is a potent inhibitor of viral replication in vivo. Short-term therapy could not prevent a rebound of viral replication after the drug was withdrawn. Preventive therapy with β -L-F-ddC could delay the onset of viremia by only 1 day compared with the time to the onset of viremia in the control group. The in vivo inhibitory effect of β -L-F-ddC was much stronger than that of ddC and was not associated with signs of toxicity. The data show that β -L-F-ddC inhibits hepadnavirus reverse transcription and is a strong inhibitor of viral replication both in vitro and in vivo.

CC 1-5 (Pharmacology)

ST fluorocytidine deriv duck **hepatitis** virus inhibition; reverse transcription **hepatitis** virus fluorocytidine deriv; DNA synthesis **hepatitis** virus fluorocytidine deriv

IT Deoxyribonucleic acid formation

Reverse transcription

Virucides and Virustats

(dideoxyfluorocytidine inhibits duck **hepatitis** B virus reverse transcription and suppresses **viral** DNA synthesis in hepatocytes both in vitro and in vivo in relation to **antiviral** activity)

IT Virus, animal

(duck **hepatitis** B, dideoxyfluorocytidine inhibits duck **hepatitis** B virus reverse transcription and suppresses **viral** DNA synthesis in hepatocytes both in vitro and in vivo in relation to **antiviral** activity)

IT 147058-39-7, β -L-F-DdC

RL: **BAC** (**Biological activity or effector, except adverse**); BSU (Biological study, unclassified); **THU** (**Therapeutic use**); BIOL (Biological study); USES (Uses)

(dideoxyfluorocytidine inhibits duck **hepatitis** B virus reverse transcription and suppresses **viral** DNA synthesis in hepatocytes both in vitro and in vivo in relation to **antiviral** activity)

IT 9068-38-6, Reverse transcriptase

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(dideoxyfluorocytidine inhibits duck **hepatitis** B virus reverse transcription and suppresses **viral** DNA synthesis in hepatocytes both in vitro and in vivo in relation to **antiviral** activity)

IT 147058-39-7, β -L-F-DdC

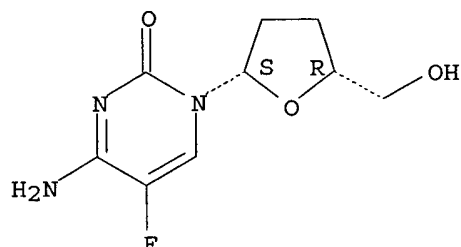
RL: **BAC** (**Biological activity or effector, except adverse**); BSU (Biological study, unclassified); **THU** (**Therapeutic use**); BIOL (Biological study); USES (Uses)

(dideoxyfluorocytidine inhibits duck **hepatitis** B virus reverse transcription and suppresses **viral** DNA synthesis in hepatocytes both in vitro and in vivo in relation to **antiviral** activity)

RN 147058-39-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L34 ANSWER 49 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:758991 HCAPLUS

DOCUMENT NUMBER: 123:237823

TITLE: Methods for the treatment of infection caused by **hepatitis** B virus (HBV)

INVENTOR(S): Adair, Dennis W.; Smiles, Kenneth A.; King, Dannie H.

PATENT ASSIGNEE(S): Oclassen Pharmaceuticals Inc., USA

SOURCE: U.S., 35 pp. Cont.-in-part of U.S. Ser. No. 952,927, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

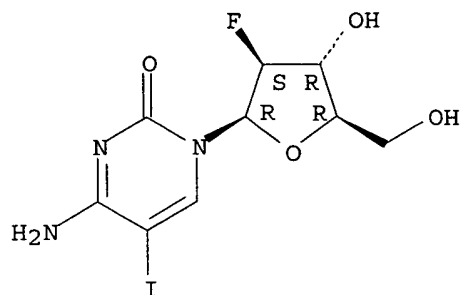
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5432165	A	19950711	US 1992-959004	19921009
IN 176739	A	19960831	IN 1993-MA203	19930222
AU 9335302	A1	19931007	AU 1993-35302	19930318
AU 662804	B2	19950914		
CA 2092356	AA	19931007	CA 1993-2092356	19930324
ZA 9302271	A	19931018	ZA 1993-2271	19930330
NO 9301246	A	19931007	NO 1993-1246	19930331
EP 565412	A1	19931013	EP 1993-400854	19930402
R: AT, CH, DE, DK, GB, IE, LI, LU, MC, NL, SE				
FR 2689398	A1	19931008	FR 1993-3979	19930405
FR 2689398	B1	19941118		
WO 9319762	A1	19931014	WO 1993-US3194	19930405
W: BB, BG, BR, CZ, FI, HU, KP, KZ, LK, MG, MN, MW, PL, RO, RU, SD, SK, UA				
RW: BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
BE 1009181	A5	19961203	BE 1993-337	19930405
ES 2105923	A1	19971016	ES 1993-698	19930405
ES 2105923	B1	19980701		
BR 9306207	A	19980623	BR 1993-6207	19930405
JP 06009403	A2	19940118	JP 1993-79849	19930406
CN 1081879	A	19940216	CN 1993-105728	19930406
LV 10191	B	19950420	LV 1993-231	19930406
IN 180270	A	19980124	IN 1995-MA27	19950109
PRIORITY APPLN. INFO.:			US 1992-863890	B2 19920406
			US 1992-952927	B2 19920925

US 1992-959004 A 19921009
IN 1993-MA203 A1 19930222
WO 1993-US3194 W 19930405

- AB The administration of low dosage amts. of 1-(2'-deoxy-2'-fluoro- β -D-arabinofuranosyl)-5-iodouracil (FIAU) to humans chronically infected with **hepatitis** B virus HBV is effective in reducing circulating markers associated with HBV. Methods of the preparation of pharmaceutical **antiviral** compns. are disclosed. Thus, a syrup was prepared containing FIAU 10, FD&C Red 40 0.025, FD&C Yellow 0.010, and FD&C Blue 1 0.001 mg, glycerin 0.10, alc 0.10, propylene glycol 0.10, and water 0.10 and artificial flavor 0.001 and maltitol syrup qs 1.0 mL. The effectiveness of the drug in treating the HBV virus was demonstrated in humans.
- IC ICM A61K031-505
- CC 63-6 (Pharmaceuticals)
- Section cross-reference(s): 1
- ST **hepatitis** B virus FIAU analog
- IT Virucides and Virustats
(**hepatitis** B virus infection treatment in humans with FIAU or analogs)
- IT Pharmaceutical dosage forms
(capsules, **hepatitis** B virus infection treatment in humans with FIAU or analogs)
- IT Pharmaceutical dosage forms
(gels, **hepatitis** B virus infection treatment in humans with FIAU or analogs)
- IT Virus, animal
(**hepatitis** B, **hepatitis** B virus infection treatment in humans with FIAU or analogs)
- IT Pharmaceutical dosage forms
(ointments, **hepatitis** B virus infection treatment in humans with FIAU or analogs)
- IT Pharmaceutical dosage forms
(ointments, creams, **hepatitis** B virus infection treatment in humans with FIAU or analogs)
- IT Pharmaceutical dosage forms
(solns., **hepatitis** B virus infection treatment in humans with FIAU or analogs)
- IT Pharmaceutical dosage forms
(syrups, **hepatitis** B virus infection treatment in humans with FIAU or analogs)
- IT Pharmaceutical dosage forms
(tablets, **hepatitis** B virus infection treatment in humans with FIAU or analogs)
- IT 69123-90-6, FIAC 69123-94-0 69123-98-4, FIAU 157695-90-4
RL: **BAC** (**Biological activity or effector, except adverse**); BSU (Biological study, unclassified); **THU** (**Therapeutic use**); BIOL (Biological study); USES (Uses)
(**hepatitis** B virus infection treatment in humans with FIAU or analogs)
- IT 69123-90-6, FIAC
RL: **BAC** (**Biological activity or effector, except adverse**); BSU (Biological study, unclassified); **THU** (**Therapeutic use**); BIOL (Biological study); USES (Uses)
(**hepatitis** B virus infection treatment in humans with FIAU or analogs)
- RN 69123-90-6 HCAPLUS
- CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy-2-fluoro- β -D-arabinofuranosyl)-5-iodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L34 ANSWER 50 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:557391 HCAPLUS

DOCUMENT NUMBER: 123:931

TITLE: Nucleosides with anti-*hepatitis* B virus activity

INVENTOR(S): Schinazi, Raymond F.; Sommadossi, Jean-Pierre; Imbach, Jean-Louis; Gosselin, Giles

PATENT ASSIGNEE(S): Emory University, USA; Center National de la Recherche Scientifique (CNRS); UAB Research Foundation

SOURCE: PCT Int. Appl., 33 pp.

CODEN: PIXXD2

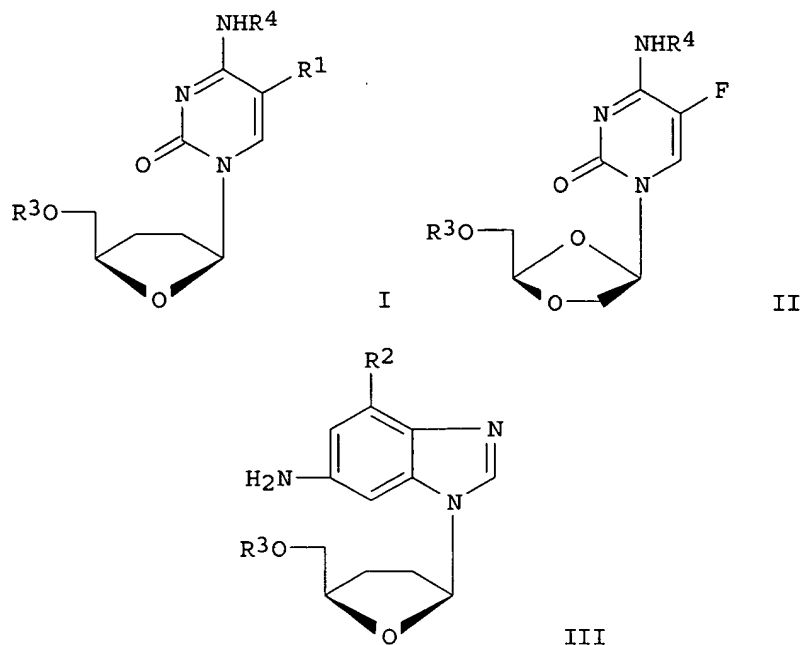
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

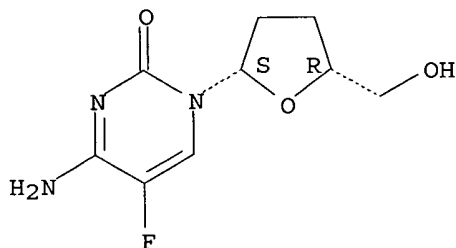
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9507086	A1	19950316	WO 1994-US10208	19940912
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2171550	AA	19950316	CA 1994-2171550	19940912
AU 9479546	A1	19950327	AU 1994-79546	19940912
EP 717628	A1	19960626	EP 1994-930421	19940912
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09504785	T2	19970513	JP 1994-508813	19940912
US 5990093	A	19991123	US 1997-829748	19970331
US 6525033	B1	20030225	US 1999-447067	19991122
PRIORITY APPLN. INFO.:				US 1993-119470 A 19930910
				WO 1994-US10208 W 19940912
				US 1994-320461 B1 19941007
				US 1995-587598 B1 19951222
				US 1997-829748 A1 19970331
OTHER SOURCE(S):		MARPAT 123:931		
GI				



- AB Infection with **hepatitis** B virus is treated by administering dideoxynucleosides or salts thereof, optionally in a pharmaceutically acceptable carrier or diluent. Thus, (+)- β -D-2-hydroxymethyl-5-(5-fluorocytosin-1-yl)-1,3-dioxolane showed an ED₅₀ against **hepatitis** B virions of 0.020 μ M and a cytotoxicity to HEPG-2 cells of 251 μ M.
- IC ICM A61K031-70
ICS C07H019-048; C07H019-16
- CC 1-5 (Pharmacology)
- ST **antiviral** cytidine nucleoside; **hepatitis** B virus inhibitor nucleoside
- IT Virucides and Virustats
(nucleosides with anti-**hepatitis** B virus activity)
- IT Nucleosides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleosides with anti-**hepatitis** B virus activity)
- IT Virus, animal
(**hepatitis** B, nucleosides with anti-**hepatitis** B virus activity)
- IT 121154-51-6, β -L-2',3'-Dideoxycytidine 145417-33-0
147058-39-7, β -L-2',3'-Dideoxy-5-fluorocytidine
RL: ADV (Adverse effect, including toxicity); **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(nucleosides with anti-**hepatitis** B virus activity)
- IT **147058-39-7**, β -L-2',3'-Dideoxy-5-fluorocytidine
RL: ADV (Adverse effect, including toxicity); **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(nucleosides with anti-**hepatitis** B virus activity)

RN 147058-39-7 HCAPLUS
CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

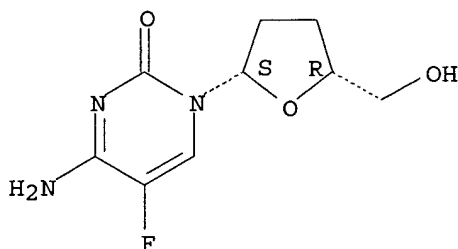
Absolute stereochemistry. Rotation (-).



L34 ANSWER 51 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:498740 HCAPLUS
DOCUMENT NUMBER: 122:306090
TITLE: Immunomodulatory and **antiviral** activities of
2',3'-dideoxy-β-L-cytidine and
2',3'-dideoxy-β-L-5-fluorocytidine
AUTHOR(S): Gagnon, L.; Nordstrom, P.A.; Duchaine, J.; Jutras, D.;
Hamel, M.; Barbeau, D.; Hooker, E.; Ashman, C.;
Cammack, N.; et al.
CORPORATE SOURCE: Virol./Immunol. Dept., BioChem Therapeutic Inc.,
Quebec, QC, H7V 4A7, Can.
SOURCE: Immunopharmacology and Immunotoxicology (1995), 17(1),
17-32
CODEN: IITOEf; ISSN: 0892-3973
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two dideoxynucleosides, 2',3'-dideoxy-β-L-cytidine and
2',3'-dideoxy-β-L-5-fluorocytidine, containing unnatural L-configuration
in their sugar moieties, were synthesized and assayed for
antiviral activities. Both compds. were shown to possess potent
anti-human immunodeficiency virus type 1 and anti-**hepatitis B**
virus activities, while demonstrating no anti-herpes simplex viruses 1 and
2 activity. These two compds. exhibited in vitro cellular toxicities for
several leukocytic cell lines and were shown to inhibit
phytohemagglutinin-stimulated human peripheral blood mononuclear leukocyte
proliferations. At inhibitory concns., both compds. caused accumulations
of cells in the S phase. While demonstrating no obvious morphol. toxicity
in vivo in mice at concns. of 75 and 150 mg/kg, 2',3'-dideoxy-β-L-5-
fluorocytidine-treated animals were shown to have considerable increases
in CD4/CD8 double pos. T lymphocyte population in their blood circulation.
CC 1-7 (Pharmacology)
ST cytidine deriv immunomodulator **antiviral**
IT Immunomodulators
Virucides and Virustats
(immunomodulatory and **antiviral** activities of dideoxycytidine
and dideoxyfluorocytidine)
IT Virus, animal
(**hepatitis B**, immunomodulatory and **antiviral**
activities of dideoxycytidine and dideoxyfluorocytidine)
IT Virus, animal
(human immunodeficiency 1, immunomodulatory and **antiviral**

activities of dideoxycytidine and dideoxyfluorocytidine)
IT 121154-51-6 147058-39-7
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); BIOL (Biological study)
(immunomodulatory and **antiviral** activities of dideoxycytidine
and dideoxyfluorocytidine)
IT 147058-39-7
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); BIOL (Biological study)
(immunomodulatory and **antiviral** activities of dideoxycytidine
and dideoxyfluorocytidine)
RN 147058-39-7 HCAPLUS
CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-
(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L34 ANSWER 52 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:207998 HCAPLUS

DOCUMENT NUMBER: 120:207998

TITLE: **Antiviral** activity of 2',3'-dideoxy-beta-L-5-fluorocytidine (beta-L-EddC) and 2',3'-dideoxy-beta-L-cytidine (beta-L-ddC) against **hepatitis** B virus and human immunodeficiency virus type 1 in vitro

AUTHOR(S): Lin, Tai Shun; Luo, Mei Zhen; Liu, Mao Chin; Pai, S. Balakrishna; Dutschman, Ginger E.; Cheng, Yung Chi

CORPORATE SOURCE: Sch. Med., Yale Univ., New Haven, CT, 06510, USA

SOURCE: Biochemical Pharmacology (1994), 47(2), 171-4

CODEN: BCPCA6; ISSN: 0006-2952

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 2',3'-Dideoxy-beta-L-5-fluorocytidine (beta-L-FddC) and 2',3'-dideoxy-beta-L-cytidine (beta-L-ddC), two nucleosides with "unnatural L-configuration," have been synthesized and found to have potent **antiviral** activity against **hepatitis** B virus (HBV) and human immunodeficiency virus type 1 (HIV-1) in vitro with very little toxicity. At 1 μ M, both beta-L-ddC and beta-L-FddC inhibited the growth of HBV by more than 90%, while at the same concentration

the

D-configuration counterparts, 2',3'-deoxy-beta-D-cytidine (ddC) and 2',3'-dideoxy-beta-D-5-fluorocytidine (beta-D-FddC), did not show **antiviral** activity against HBV. The order of anti-HIV-1 activity was beta-D-FddC > ddC; beta-D-FddC > beta-L-ddC. The dose limiting toxicity of ddC is neuropathy which is believed to be caused by the inhibition of the synthesis of mitochondrial DNA. DdC severely inhibited the mitochondrial DNA synthesis of CEM cells yielding an IC50 value of

0.022 μ M. Conversely, both β -L-FddC and β -L-ddC did not demonstrate any inhibition against mitochondrial DNA synthesis up to 100 μ M concentration

CC 1-5 (Pharmacology)

ST **antiviral hepatitis** HIV1 dideoxyfluorocytidine dideoxycytidine

IT Virucides and Virustats
(dideoxycytidine and dideoxyfluorocytidine L-isomers, against **hepatitis** B and HIV-1)

IT Virus, animal
(**hepatitis** B, inhibition of, by dideoxycytidine and dideoxyfluorocytidine L-isomers)

IT 7481-89-2 **107036-62-4**

RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**antiviral** activity of, enantiomer comparison with)

IT 121154-51-6P **147058-39-7P**

RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation and **antiviral** activity of, against **hepatitis** B and HIV-1)

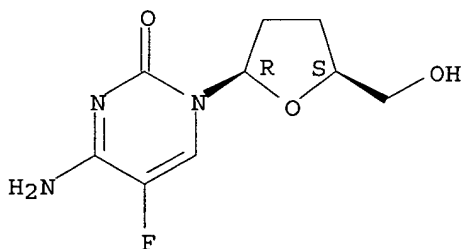
IT **107036-62-4**

RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**antiviral** activity of, enantiomer comparison with)

RN 107036-62-4 HCAPLUS

CN Cytidine, 2',3'-dideoxy-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **147058-39-7P**

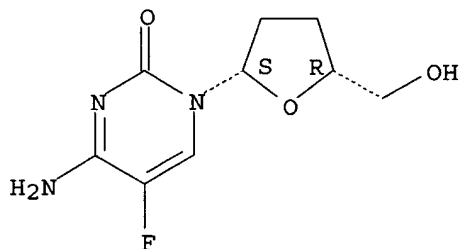
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation and **antiviral** activity of, against **hepatitis** B and HIV-1)

RN 147058-39-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L34 ANSWER 53 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:561 HCAPLUS

DOCUMENT NUMBER: 120:561

TITLE: Treating **hepatitis** B virus infections using 1-(2'-deoxy-2'-fluoro-beta-D-arabinofuranosyl)-5-methyluracil (FMAU).

INVENTOR(S): Fox, Jack J.; Watanabe, Kyoichi A.; Lopez, Carlos; Trepo, Christian G.

PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA; Institut National de la Sante et de la Recherche Medicale (INSERM)

SOURCE: U.S., 27 pp. Cont. of U.S. Ser. No. 318,602 abandoned. CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5246924	A	19930921	US 1991-700334	19910506
CA 1328865	A1	19940426	CA 1988-576381	19880902
PRIORITY APPLN. INFO.:			US 1987-92446	B2 19870903
			CA 1988-576381	A 19880902
			US 1989-318602	B1 19890303

AB A method for treating infection caused by **hepatitis** B virus or woodchuck **hepatitis** virus comprises administering 0.04-2mg/Kg FMAU or its salt. Thus, **antiviral** effects of FMAU, FEAU [1-(2'-deoxy-2'-fluoro-beta-D-arabinofuranosyl)-5-ethyluracil], and EDU [1-(2'-deoxy-beta-D-arabinofuranosyl)-5-ethyluracil] were tested in mice inoculated intracerebrally with herpes simplex virus 2. DNA polymerase of human **hepatitis** virus and woodchuck **hepatitis** virus was inhibited by the nucleotide triphosphate analogs, i.e. FMA-UTP, FIA-CTP, BVdUTP, ara-TTP, ACVTP, and ara-CTP.

IC ICM A61K031-70

INCL 514050000

CC 1-5 (Pharmacology)

ST **hepatitis** B virus virucide fluoroarabinofuranosylethyluracil; arabinofuranosylethyluracil deoxyarabinofuranosylethyluracil **hepatitis** B treatment

IT **Hepatitis**

(treatment of, fluoroarabinofuranosylmethyluracil for)

IT **Hepatitis**

(B, treatment of, fluoroarabinofuranosylmethyluracil for)

IT Pharmaceutical dosage forms

(injections, i.v., fluoroarabinofuranosylmethyluracil-containing, for treating **hepatitis** B virus infection)

IT Pharmaceutical dosage forms
(oral, fluoroarabinofuranosylmethyluracil-containing, for treating
hepatitis B virus infection)

IT 15176-29-1 **69123-90-6** 69123-98-4 69256-17-3 83546-42-3
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); USES (Uses)
(**hepatitis B virus infection treatment with**)

IT 13191-15-6 66097-68-5, Ara-TTP 66341-18-2 77222-61-8 79551-89-6
79570-63-1
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); BIOL (Biological study)
(inhibition of DNA polymerase of **hepatitis** virus with)

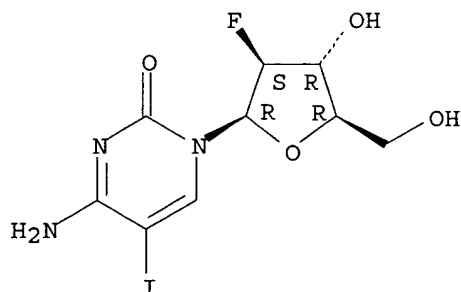
IT 9012-90-2, DNA polymerase
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological
study, unclassified); BIOL (Biological study)
(inhibition of, of **hepatitis** virus,
fluoroarabinofuranosylmethyluracil for)

IT **69123-90-6**
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); USES (Uses)
(**hepatitis B virus infection treatment with**)

RN 69123-90-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-
5-iodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

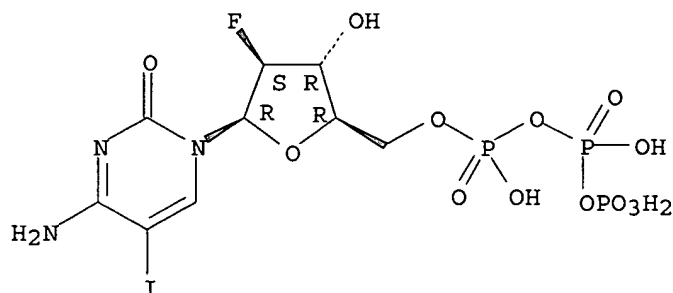


IT **79570-63-1**
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); BIOL (Biological study)
(inhibition of DNA polymerase of **hepatitis** virus with)

RN 79570-63-1 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-[2-deoxy-2-fluoro-5-O-
[hydroxy[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-β-D-
arabinofuranosyl]-5-iodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L34 ANSWER 54 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:33948 HCAPLUS

DOCUMENT NUMBER: 118:33948

TITLE: Methods of screening for transcriptional modulators and for transcriptional modulation of gene expression

INVENTOR(S): Foulkes, J. Gordon; Case, Casey C.; Leichtfried, Franz; Pieler, Christian; Stephenson, John

PATENT ASSIGNEE(S): Oncogene Science, Inc., USA

SOURCE: PCT Int. Appl., 166 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9212635	A1	19920806	WO 1992-US424	19920117
W: AU, CA, FI, HU, JP, KR, NO, RU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
AU 9213472	A1	19920827	AU 1992-13472	19920117
US 6203976	B1	20010320	US 1994-255236	19940607
US 6165712	A	20001226	US 1995-463691	19950605
PRIORITY APPLN. INFO.:			US 1991-644233	A2 19910118
			US 1989-382712	B2 19890718
			US 1990-555196	B2 19900718
			WO 1992-US424	A 19920117
			US 1994-255236	A3 19940607

AB A method for directly modulating, using an exogenous compound, transcription of a viral gene, the product of which is associated with a physiol. or pathol. state of the host cell or multicellular organism, is disclosed. The method can also be used for modulating the expression of a gene encoding a desirable protein product. A method for screening transcription inducers or inhibitors using the luciferase gene fused with a promoter of yeast, virus, or animal cells as a reporter was described. Approx. 100 chems. (of 2000 tested) which selectively modulated gene expression were identified.

IC ICM A01N043-04

ICS C12N015-11; C12P021-00; C12Q001-66; C12Q001-68; C12Q001-70

CC 3-1 (Biochemical Genetics)

Section cross-reference(s): 14

IT Virucides and Virustats

(modulators for viral gene transcription as, method for screening for compds. for use as)

IT Neoplasm inhibitors

- (modulators of **viral** gene transcription as, method for screening of compds. for use as)
- IT Transcription, genetic
 - (of **viral** and other genes, modulation of, screening of compds. for use in)
- IT Acquired immune deficiency syndrome
 - Hepatitis**
 - Influenza
 - Measles
 - Mumps
 - Poliomyelitis
 - Rubella
 - (treatment of, modulators of **viral** gene transcription for, method for screening of compds. for use as)
- IT Nucleic acids
 - RL: BIOL (Biological study)
 - (triple helix-forming, for **viral** and other genes transcription modulation, screening of compds. for use in)
- IT Leukemia
 - Neoplasm
 - (**viral** gene associated with, modulation of transcription of, screening of compds. for use in)
- IT Therapeutics
 - (**viral** gene transcriptional modifiers for, method for screening compds. for use as)
- IT Infection
 - (**viral**, treatment of, modulation of **viral** gene transcription for, screening of compds. for use in)
- IT Virus, animal
 - (Epstein-Barr, infection by, treatment of, modulation of **viral** gene transcription for, screening of compds. for use in)
- IT Virus, animal
 - (adeno-, infection by, treatment of, modulation of **viral** gene transcription for, screening of compds. for use in)
- IT Ribonucleic acids
 - RL: BIOL (Biological study)
 - (antisense, for **viral** and other genes transcription modulation, screening of compds. for use in)
- IT Virus, animal
 - (arbo-, infection by, treatment of, modulation of **viral** gene transcription for, screening of compds. for use in)
- IT Neoplasm inhibitors
 - (cervix carcinoma, modulators of **viral** gene transcription as, method for screening of compds. for use as)
- IT Uterus, neoplasm
 - (cervix, carcinoma, **viral** gene associated with, modulation of transcription of, screening of compds. for use in)
- IT Uterus, neoplasm
 - (cervix, carcinoma, inhibitors, modulators of **viral** gene transcription as, method for screening of compds. for use as)
- IT Deoxyribonucleic acids
 - RL: BIOL (Biological study)
 - (complementary, antisense, for **viral** and other genes transcription modulation, screening of compds. for use in)
- IT Virus, animal
 - (cytomegalo-, infection by, treatment of, modulation of **viral** gene transcription for, screening of compds. for use in)
- IT Virus, animal
 - (echo, infection by, treatment of, modulation of **viral** gene

- transcription for, screening of compds. for use in)
- IT Virus, animal
 - (**hepatitis**, infection by, treatment of, modulation of **viral** gene transcription for, screening of compds. for use in)
- IT Neoplasm inhibitors
 - (hepatoma, modulators of **viral** gene transcription as, method for screening of compds. for use as)
- IT Liver, neoplasm
 - (hepatoma, **viral** gene associated with, modulation of transcription of, screening of compds. for use in)
- IT Liver, neoplasm
 - (hepatoma, inhibitors, modulators of **viral** gene transcription as, method for screening of compds. for use as)
- IT Virus, animal
 - (herpes, infection by, treatment of, modulation of **viral** gene transcription for, screening of compds. for use in)
- IT Skin, disease
 - (herpes, treatment of, modulators of **viral** gene transcription for, method for screening of compds. for use as)
- IT Virus, animal
 - (human T-cell leukemia, infection by, treatment of, modulation of **viral** gene transcription for, screening of compds. for use in)
- IT Virus, animal
 - (human immunodeficiency 1, infection by, treatment of, modulation of **viral** gene transcription for, screening of compds. for use in)
- IT Mononucleosis
 - (infectious, treatment of, modulators of **viral** gene transcription for, method for screening of compds. for use as)
- IT Virus, animal
 - (influenza, infection by, treatment of, modulation of **viral** gene transcription for, screening of compds. for use in)
- IT Pharmaceutical dosage forms
 - (injections, i.m., i.m. or s.c., modulators for **viral** gene transcription in, method for screening for compds. for use as)
- IT Pharmaceutical dosage forms
 - (injections, i.v., modulators for **viral** gene transcription in, method for screening for compds. for use as)
- IT Neoplasm inhibitors
 - (leukemia, modulators of **viral** gene transcription as, method for screening of compds. for use as)
- IT Virus, animal
 - (measles, infection by, treatment of, modulation of **viral** gene transcription for, screening of compds. for use in)
- IT Animal tissue culture
 - (monolayer, screening of compds. for modulation of transcription of **viral** and other genes in)
- IT Virus, animal
 - (mumps, infection by, treatment of, modulation of **viral** gene transcription for, screening of compds. for use in)
- IT Pharmaceutical dosage forms
 - (oral, modulators for **viral** gene transcription in, method for screening for compds. for use as)
- IT Virus, animal
 - (papilloma, infection by, treatment of, modulation of **viral** gene transcription for, screening of compds. for use in)
- IT Virus, animal
 - (parainfluenza, infection by, treatment of, modulation of **viral** gene transcription for, screening of compds. for use in)
- IT Virus, animal

(parvo-, infection by, treatment of, modulation of **viral** gene transcription for, screening of compds. for use in)

IT Virus, animal
(polio-, infection by, treatment of, modulation of **viral** gene transcription for, screening of compds. for use in)

IT Virus, animal
(respiratory syncytial, infection by, treatment of, modulation of **viral** gene transcription for, screening of compds. for use in)

IT Virus, animal
(rhino-, infection by, treatment of, modulation of **viral** gene transcription for, screening of compds. for use in)

IT Virus, animal
(rota-, infection by, treatment of, modulation of **viral** gene transcription for, screening of compds. for use in)

IT Virus, animal
(rubella, infection by, treatment of, modulation of **viral** gene transcription for, screening of compds. for use in)

IT Animal tissue culture
(suspension, screening of compds. for modulation of transcription of **viral** and other genes in)

IT Pharmaceutical dosage forms
(topical, modulators for **viral** gene transcription in, method for screening for compds. for use as)

IT Pharmaceutical dosage forms
(transdermal, modulators for **viral** gene transcription in, method for screening for compds. for use as)

IT Virus, animal
(varicella-zoster, infection by, treatment of, modulation of **viral** gene transcription for, screening of compds. for use in)

IT 50-24-8 52-21-1 56-75-7 57-68-1 59-14-3 65-45-2 65-61-2
69-05-6 76-25-5 76-60-8 88-44-8 90-90-4 93-40-3 96-50-4,
2-Thiazolamine 104-83-6 108-78-1, 1,3,5-Triazine-2,4,6-triamine,
biological studies 110-89-4, Piperidine, biological studies 112-82-3
119-63-1 134-50-9 135-20-6 138-37-4 153-78-6, 9H-Fluoren-2-amine
154-42-7 290-87-9, 1,3,5-Triazine 305-84-0 464-45-9 464-48-2
480-16-0 490-59-5, Benzo[g]pteridine-2,4(1H,3H)-dione 519-34-6
528-48-3 548-62-9 550-82-3 555-44-2 581-64-6 585-70-6 623-00-7
722-27-0 822-87-7 873-63-2 915-67-3 **1022-79-3** 1072-83-9
1141-88-4 1148-79-4, 2,2':6',2''-Terpyridine 1155-64-2 1260-17-9
1324-21-6, C.I. Mordant Black 13 1437-15-6 1746-81-2 1779-81-3
1817-73-8 1837-57-6 1918-02-1 1932-03-2 2051-98-1 2113-57-7
2411-89-4 2465-27-2 2466-76-4 2946-39-6 3096-57-9 3398-16-1
3564-17-8 3564-73-6 3721-95-7, Cyclobutanecarboxylic acid 3972-65-4
4016-63-1 5056-12-2, 4'-Apo- β , ψ -carotenal 5413-85-4
5427-26-9 6952-59-6 10045-45-1 10510-54-0 11121-48-5, Rose Bengal
13808-64-5 14548-46-0 17026-42-5 17687-22-8 19752-55-7
22509-74-6 25005-96-3 34161-31-4 36192-63-9 38026-46-9
42580-42-7 46242-90-4 52547-00-9 52698-84-7 54057-95-3
54327-10-5, Methyl green 54375-47-2 54512-75-3 58253-99-9
59895-79-3 61540-35-0 64700-15-8 74266-66-3 86130-54-3
88404-25-5 88738-78-7 102185-49-9 123333-82-4 138255-65-9
138313-25-4 145177-89-5 145177-90-8 145177-91-9 145177-93-1
145177-94-2 145268-20-8, Arnica 4X
RL: **BAC** (**Biological activity or effector, except adverse**); BPR
(Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
(transcriptional activator in mammalian cell culture)

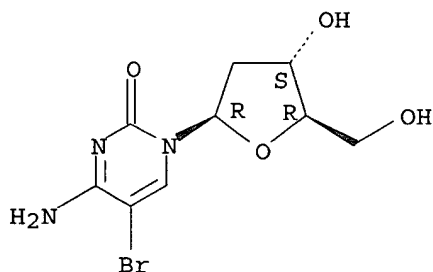
IT **1022-79-3**
RL: **BAC** (**Biological activity or effector, except adverse**); BPR

(Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
(transcriptional activator in mammalian cell culture)

RN 1022-79-3 HCAPLUS

CN Cytidine, 5-bromo-2'-deoxy- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L34 ANSWER 55 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:563386 HCAPLUS

DOCUMENT NUMBER: 117:163386

TITLE: Effects of 2'-fluorinated arabinosyl-pyrimidine nucleosides on duck *hepatitis* B virus DNA level in serum and liver of chronically infected ducks
AUTHOR(S): Fourel, I.; Li, J.; Hantz, O.; Jacquet, C.; Fox, J. J.; Trepo, C.

CORPORATE SOURCE: INSERM, Lyon, Fr.

SOURCE: Journal of Medical Virology (1992), 37(2), 122-6
CODEN: JMVIDB; ISSN: 0146-6615

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The 2'-fluorinated arabinosyl-pyrimidine nucleosides, 1-(2'-deoxy-2'-fluoro-β-D-arabinofuranosyl)-5-iodocytosine (FIAC) and 1-(2'-deoxy-2'-fluoro-β-D-arabinofuranosyl)-5-methyluracil (FMAU), are 2 new **antiviral** compds. with in vitro inhibitory activity against the DNA polymerase of hepadnaviruses. Those compds. also induced permanent inhibition of viral replication in woodchucks chronically infected by woodchuck *hepatitis* virus. The effects of these **antiviral** compds. were assessed in ducks chronically infected by duck *hepatitis* B virus (DHBV). Following i.p. administration for 5 days, FMAU (2 mg/kg/day) and FIAC (10 mg/kg/day) induced a transient decrease in DHBV replication, as shown by the decrease in both the serum and live DHBV DNA level. After stopping therapy, DHBV replication rebounded immediately to the pretreatment level. The supercoiled form of liver viral DNA was found to be less affected by the therapy. By contrast, no obvious **antiviral** effect was observed with vidarabine monophosphate (ara-AMP) (80 mg/kg/day) therapy. No sign of toxicity was observed during the course of the treatment. These preliminary results confirmed in the DHBV model the higher efficacy of FIAC and FMAU as compared to ara-AMP. Pharmacokinetic studies are needed to explain the differences observed in viral replication in these 2 models of HBV infection.

CC 1-5 (Pharmacology)

ST **antiviral** fluorinated arabinosyl pyrimidine nucleoside; deoxyfluoroarabinofuranosylmethyluracil duck *hepatitis* B virus DNA; deoxyfluoroarabinofuranosyliodocytosine duck *hepatitis* B virus DNA

IT Virucides and Virustats
(fluorinated arabinosyl-pyrimidine nucleosides as, against duck **hepatitis** B virus)

IT Deoxyribonucleic acids
RL: BIOL (Biological study)
(of duck **hepatitis** B virus, in serum and liver of infected ducks, fluorinated arabinosyl-pyrimidine nucleosides effects on)

IT Virus, animal
(duck **hepatitis** B, DNA, of serum and liver infected ducks, fluorinated arabinosyl-pyrimidine nucleoside effects on)

IT Nucleosides, biological studies
RL: BIOL (Biological study)
(pyrimidine, fluorinated arabinosyl-, **antiviral** activity of, against duck **hepatitis** B virus)

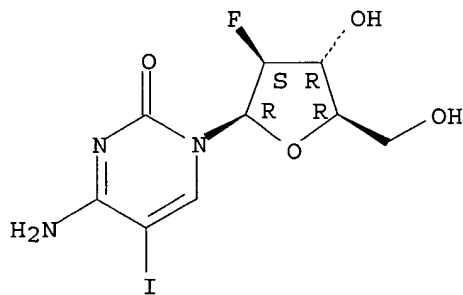
IT 69123-90-6 69256-17-3
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**antiviral** activity of, against duck **hepatitis** B virus)

IT 69123-90-6
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**antiviral** activity of, against duck **hepatitis** B virus)

RN 69123-90-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy-2-fluoro- β -D-arabinofuranosyl)-5-iodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L34 ANSWER 56 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:400329 HCAPLUS

DOCUMENT NUMBER: 117:329

TITLE: Inhibition of **hepatitis** B virus production by modified 2',3'-dideoxythymidine and 2',3'-dideoxy-5-methylcytidine derivatives. In vitro and in vivo studies

AUTHOR(S): Matthes, E.; Von Janta-Lipinski, M.; Will, H.; Schroeder, H. C.; Merz, H.; Steffen, R.; Mueller, W. E. G.

CORPORATE SOURCE: Inst. Molekularbiol., Berlin-Buch, 1115, Germany

SOURCE: Biochemical Pharmacology (1992), 43(7), 1571-7

CODEN: BCPCA6; ISSN: 0006-2952

DOCUMENT TYPE: Journal
LANGUAGE: English

- AB The effect of analogs of both 2',3'-dideoxy-3'-fluorothymidine (FddThd) [2',3'-dideoxy-3'-fluorouridine (FddUrd), 2',3'-dideoxy-3'-fluoro-5-chlorouridine (FddClUrd), 2',3'-dideoxy-3'-fluoro-5-bromouridine (FddBrUrd) and 2',3'-dideoxy-3'-fluoro-5-bromovinyluridine (FddBVUrd)] and 2',3'-dideoxy-3'-fluorocytidine (FddCyt) [2',3'-dideoxy-3'-fluoro-5-fluorocytidine (FddFCyt), 2',3'-dideoxy-3'-fluoro-5-chlorocytidine (FddClCyt), 2',3'-dideoxy-3'-fluoro-5-methylcytidine (FddMeCyt), 2',3'-dideoxy-3'-fluoro-5-ethylcytidine (FddEtCyt), 2',3'-dideoxy-3'-chloro-5-methylcytidine (ClddMeCyt), 2',3'-dideoxy-3'-amino-5-methylcytidine (AmddMeCyt), 2',3'-dideoxy-3'-azido-5-methylcytidine (AzddMeCyt) and arabinosyl-5-methylcytosine (AraMeCyt)] were tested for their potential **antiviral** activity in vitro using the human hepatoblastoma cell line, Hep G2 2.2.15, which was transfected with a vector containing **hepatitis B virus (HBV)**. It was found that FddThd, FddMeCyt, FddEtCyt, ClddMeCyt, AmddMeCyt and AraMeCyt display cytostatic activity at concns. (CD50 values) between 0.54 (FddMeCyt) and 3.93 μ M (FddEtCyt), while FddUrd, FddClUrd, FddBrUrd, FddBVUrd, FddCyt, FddFCyt, FddClCyt and AzddMeCyt do not affect cell growth at concns. of up to 25 μ M. Among the thymidine analogs tested, FddThd is the most effective **antiviral** agent: at a concentration of 0.03 μ M a >90% reduction of HBV DNA synthesis was measured. On the other hand, the **antiviral** indexes displayed by FddClUrd, FddBrUrd and FddBVUrd are higher than that of FddThd; FddUrd was completely inactive. The most powerful **antiviral** agents in the group of cytidine analogs tested in vitro were FddMeCyt (>90% reduction of HBV DNA synthesis at 0.10 μ M) and ClddMeCyt (0.10 μ M); FddClCyt, FddEtCyt, AmddMeCyt and AraMeCyt were of intermediate activity. None or negligible **antiviral** activity was determined for FddUrd, FddCyt, FddFCyt and AzddMeCyt. FddThd and FddMeCyt displayed in vivo an **antiviral** effect in the duck/duck HBV (DHBV) animal system. Administration of 10 or 20 mg/kg (total daily dose) of FddThd and 5 or 10 mg/kg of FddMeCyt (i.m. daily) to ducks infected with DHBV for 12 days blocked virus production. Termination of treatment with FddThd of infected animals led to reappearance of the virus in the serum though at lower levels. The in vitro and the in vivo data suggest that FddThd and FddMeCyt might be promising **antiviral** agents for the treatment of infection caused by HBV in humans.
- CC 1-5 (Pharmacology)
- ST **hepatitis B virus dideoxythymidine dideoxymethylcytidine deriv;**
antiviral hepatitis B virus nucleoside analog
- IT Virucides and Virustats
(dideoxythymidine and dideoxymethylcytidine derivs., against **hepatitis B virus**, in human cells and duck model)
- IT Virus, animal
(duck **hepatitis B**, infection with, dideoxythymidine and dideoxymethylcytidine derivs. inhibition of, as **hepatitis B virus** animal model)
- IT Virus, animal
(**hepatitis B**, infection with, dideoxythymidine and dideoxymethylcytidine derivs. inhibition of, in human cells)
- IT 6829-31-8 25526-93-6 41107-56-6, 2',3'-Dideoxy-3'-fluorouridine
51246-79-8, 2',3'-Dideoxy-3'-fluorocytidine 87190-79-2 87190-81-6
115249-86-0, 2',3'-Dideoxy-3'-fluoro-5-bromouridine 115249-95-1
119644-22-3, 2',3'-Dideoxy-3'-fluoro-5-chlorouridine 127492-32-4
131167-83-4 134379-78-5 141645-98-9 141724-69-8
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL

(Biological study); USES (Uses)
(**antiviral** activity of, against **hepatitis B virus**
in human cells and duck model)

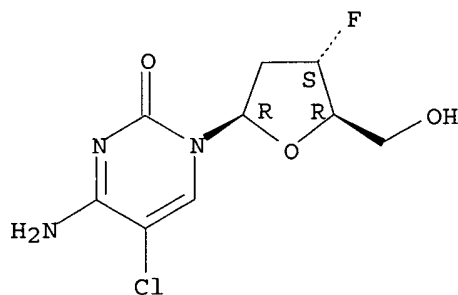
IT 127492-32-4 134379-78-5

RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); USES (Uses)
(**antiviral** activity of, against **hepatitis B virus**
in human cells and duck model)

RN 127492-32-4 HCAPLUS

CN Cytidine, 5-chloro-2',3'-dideoxy-3'-fluoro- (9CI) (CA INDEX NAME)

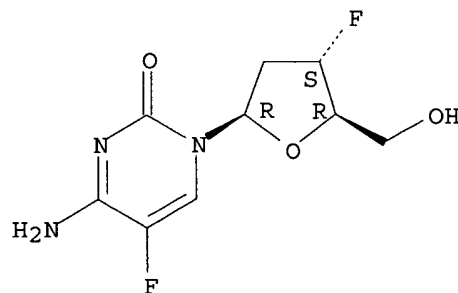
Absolute stereochemistry.



RN 134379-78-5 HCAPLUS

CN Cytidine, 2',3'-dideoxy-3',5-difluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L34 ANSWER 57 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:559680 HCAPLUS

DOCUMENT NUMBER: 115:159680

TITLE: Preparation of **antiviral** pyrimidine and
purine nucleosides and pharmaceutical compositions
containing them

INVENTOR(S): Matthes, Eckart; Von Janta-Lipinski, Martin; Reimer,
Karen; Mueller, Werner; Meisel, Helga; Lehmann,
Christine; Schildt, Juergen

PATENT ASSIGNEE(S): Akademie der Wissenschaften der DDR, Ger. Dem. Rep.

SOURCE: Eur. Pat. Appl., 19 pp.

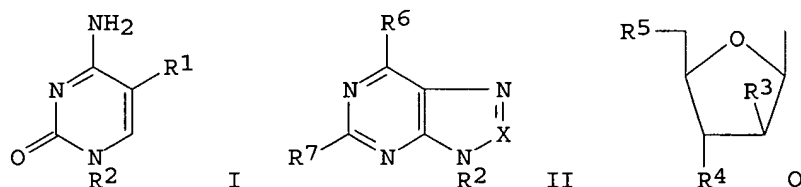
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 409227	A2	19910123	EP 1990-113851	19900719
EP 409227	A3	19911204		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DD 293498	A5	19910905	DD 1989-331051	19890720
JP 03148292	A2	19910625	JP 1990-191856	19900719
PRIORITY APPLN. INFO.:			DD 1989-331051	A 19890720
OTHER SOURCE(S):	MARPAT 115:159680			

GI



AB The title compds. [I; II; R1 = CHO, NH₂, OH, SH, halo, etc.; R2 = 2,3-didehydro-2,3-dideoxyribofuranosyl, arabinofuranosyl, Q; R3 = H, OH; R4 = H, F, Cl, NH₂, N₃; R5 = OH, OAc, palmitoyloxy, alkanoyloxy, etc.; R6, R7 = H, OH, F, Cl, Br, NH₂ SH, etc.; X = CH, N], especially useful against **hepatitis B** virus, were prepared. 1-(5-O-Acetyl-2,3-dideoxy-3-fluoro-β-D-ribofuranosyl)-5-methyl-cytosine in CCl₄ was treated over 6 h with Br under illumination from a photolamp at reflux; the product was refluxed with MeOH containing MeONa for 20 min to give 1-(2,3-dideoxy-3-fluoro-β-D-ribofuranosyl)-5-formylcytosine. Most I and II showed ID₅₀ of 0.04-26 μM against **hepatitis B** virus polymerase. Tablets and injections containing I and II were formulated.

IC ICM C07H019-04
 ICS A61K031-70

CC 33-9 (Carbohydrates)

ST Section cross-reference(s): 1, 63
 nucleoside purine pyrimidine prepn **antiviral**; **hepatitis B** virus inhibitor

IT Nucleosides, preparation
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (2',3'-dideoxyribo-, purine, preparation of, as **antivirals**)

IT Virus, animal
 (**hepatitis B**, inhibitors, purine and pyrimidine nucleosides as)

IT 6829-31-8P 7057-48-9P 115249-88-2P 120826-44-0P 131167-83-4P
 134379-73-0P 134379-74-1P 134379-75-2P 134379-76-3P 134379-77-4P
 134379-78-5P 134379-79-6P 134379-81-0P
 RL: **BAC** (**B**iological **a**ctivity or **e**ffector, **e**xcept **a**dverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (preparation of, as **antiviral**)

IT 6746-31-2 22423-28-5 87412-13-3 115249-95-1 124616-27-9
 134379-84-3 134379-85-4 134379-86-5 134379-87-6
 RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction of, in preparation of **antiviral** nucleosides)

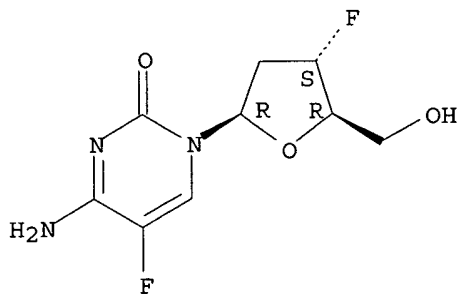
IT 134379-78-5P 134379-79-6P

RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); SPN (Synthetic preparation); BIOL
(Biological study); PREP (Preparation)
(preparation of, as **antiviral**)

RN 134379-78-5 HCAPLUS

CN Cytidine, 2',3'-dideoxy-3',5-difluoro- (9CI) (CA INDEX NAME)

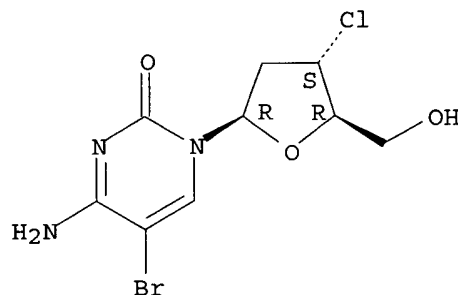
Absolute stereochemistry.



RN 134379-79-6 HCAPLUS

CN Cytidine, 5-bromo-3'-chloro-2',3'-dideoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L34 ANSWER 58 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1990:544908 HCAPLUS

DOCUMENT NUMBER: 113:144908

TITLE: Inhibition of **hepatitis** A virus replication
in vitro by **antiviral** compounds

AUTHOR(S): Crance, J. M.; Biziagos, E.; Passagot, J.; Van
Cuyck-Gandre, H.; Deloince, R.

CORPORATE SOURCE: Unite Biol. Mol., Cent. Rech. Serv. Sante Armees, La
Tronche, 38702, Fr.

SOURCE: Journal of Medical Virology (1990), 31(2), 155-60
CODEN: JMVIDB; ISSN: 0146-6615

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Forty **antiviral** compds. were screened for inhibitory effect on
hepatitis A virus (HAV) antigen expression in the human hepatoma
cell line PLC/PRF/5. Ribavirin, amantadine, glycyrrhizin, and pyrazofurin

were selected in this screening test and were studied further. The selectivity indexes of these four compds., calculated as the ratio of 50% cytotoxic dose (determined by the trypan blue exclusion and by inhibition of [3H]leucine incorporation) to the 50% ED (determined by the viral antigen expression), were 4.6 and 3.0 with ribavirin, 5.3 and 5.9 with amantadine, 15.2 and 16.9 with glycyrrhizin, and 45.4 and 74.6 with pyrazofurin. All four compds. resulted in concentration-dependent redns. of HAV antigen

expression

and HAV infectivity. Ribavirin, amantadine, pyrazofurin, and glycyrrhizin emerged, from the present study, as promising candidates for chemotherapy of acute **hepatitis A**.

CC 1-5 (Pharmacology)

ST **antiviral hepatitis A virus**; ribavirin

antiviral hepatitis A virus; amantadine

antiviral hepatitis A virus; glycyrrhizin

antiviral hepatitis A virus; pyrazofurin

antiviral hepatitis A virus

IT Virucides and Virustats

(against **hepatitis A virus**, screening for, in human hepatoma cells)

IT Saponins

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**antiviral** activity of, against **hepatitis A virus**, in human hepatoma cells)

IT Virus, animal

(**hepatitis A**, infection with, **antiviral** screening for therapy of, in human hepatoma cells)

IT Pentosans

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(sulfates, **antiviral** activity of, against **hepatitis A virus**, in human hepatoma cells)

IT 50-02-2, Dexamethasone 50-23-7, Hydrocortisone 50-81-7, Ascorbic acid, biological studies 54-21-7, Sodium salicylate 54-25-1, 6-Azaauridine 58-08-2, Caffeine, biological studies 58-32-2, Dipyridamole 66-81-9, Cycloheximide 73-03-0, Cordycepin 85-31-4, 6-Mercaptoguanosine 89-83-8 113-00-8, Guanidine 141-84-4, Rhodanine 154-23-4, Catechin 320-67-2, 5-Azacytidine 378-44-9, Betamethasone 480-18-2, Taxifolin 768-94-5, Amantadine 1024-99-3, 5-Iodouridine 1123-54-2, 8-Azaadenine 1147-23-5, 5-Iodocytidine 1397-89-3, Amphotericin B 1405-86-3, Glycyrrhizin 1445-07-4, Pseudouridine 6990-06-3, Fusidic acid 6998-60-3, Rifamycin 9005-49-6, Heparin, biological studies 9042-14-2, Dextran sulfate 9072-19-9, Fucoidan 11089-65-9, Tunicamycin 13292-46-1, Rifampicin 13877-76-4 23205-42-7, 3-Deazauridine 26001-38-7, 8-Mercaptoguanosine 30868-30-5, Pyrazofurin 36791-04-5, Ribavirin

RL: BAC (**Biological activity or effector, except adverse**); BSU (Biological study, unclassified); THU (**Therapeutic use**); BIOL (Biological study); USES (Uses)

(**antiviral** activity of, against **hepatitis A virus**, in human hepatoma cells)

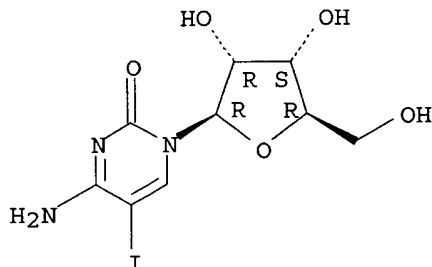
IT 1147-23-5, 5-Iodocytidine

RL: BAC (**Biological activity or effector, except adverse**); BSU (Biological study, unclassified); THU (**Therapeutic use**); BIOL (Biological study); USES (Uses)

(**antiviral** activity of, against **hepatitis A virus**,

in human hepatoma cells)
RN 1147-23-5 HCAPLUS
CN Cytidine, 5-iodo- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L34 ANSWER 59 OF 59 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1987:60841 HCAPLUS

DOCUMENT NUMBER: 106:60841

TITLE: Comparative efficacy of three 2'-fluoropyrimidine nucleosides and 9-(1,3-dihydroxy-2-propoxymethyl)guanine (BW B759U) against pseudorabies and equine rhinopneumonitis virus infection in vitro and in laboratory animals

AUTHOR(S): Rollinson, Elizabeth A.

CORPORATE SOURCE: Coppers Anim. Health Ltd., Berkhamsted/Hertfordshire, HP4 2QE, UK

SOURCE: Antiviral Research (1987), 7(1), 25-33

CODEN: ARSRDR; ISSN: 0166-3542

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The 3 2'-fluoropyrimidine nucleosides 1-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-5-iodocytosine (FIAC) [69123-90-6], 1-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-5-iodouracil (FIAU) [69123-98-4], and 1-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-5-methyluracil (FMAU) [69256-17-3], showed high activity in RK13 monolayers against equine rhinopneumonitis virus, (EHV-1), Aujeszky's disease virus (SHV-1, pseudorabies), and infectious bovine rhinotracheitis virus (IBR, BHV-1). The activity of these compds. was compared with 9-(1,3-dihydroxy-2-propoxymethyl)guanine (BW B759U, DHPG) in 2 laboratory animal

disease models: EHV-1-induced **hepatitis** in hamsters and SHV-1-induced encephalitis in mice. All the compds., provided from 3 to 5 h pre-infection for 5 days, were effective in preventing EHV-1 mortality (at 3-5 mg/kg per day) and in significantly reducing SHV-1 mortality (at 60 mg/kg per day). While FIAU had the greatest activity in vitro, FMAU tended to be more potent in vivo. The reasons for these differences between relative in vitro and in vivo activities are briefly discussed.

CC 1-5 (Pharmacology)

ST fluoropyrimidine nucleoside **antiviral**; pseudorabies virus infection fluoropyrimidine nucleoside; equine rhinopneumonitis virus fluoropyrimidine nucleoside

IT Nucleosides, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(fluoropyrimidine, **antiviral** activity of, against pseudorabies and equine rhinopneumonitis virus)

IT 69123-90-6 69123-98-4, 1-(2-Deoxy-2-fluoro-β-D-arabinofuranosyl)-5-iodouracil 69256-17-3, 1-(2-Deoxy-2-fluoro-β-D-arabinofuranosyl)-5-methyluracil

RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(**antiviral** activity of, against pseudorabies and equine rhinopneumonitis virus)

IT 69123-90-6

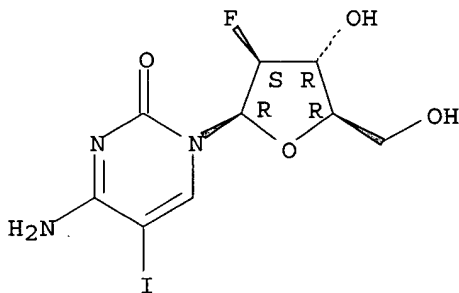
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(**antiviral** activity of, against pseudorabies and equine rhinopneumonitis virus)

RN 69123-90-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-5-iodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d que 136

L2 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

L4 109180 SEA FILE=REGISTRY SSS FUL L2

L9 17230 SEA FILE=CAPLUS ABB=ON PLU=ON L4 (L) (PAC OR THU OR BAC OR PKT OR DMA)/RL

L10 12372 SEA FILE=HCAPLUS ABB=ON PLU=ON (HCV+PFT/CT OR "CLASSICAL SWINE FEVER VIRUS"+PFT/CT OR "HEPATITIS C VIRUS"+PFT/CT)

L11 11667 SEA FILE=HCAPLUS ABB=ON PLU=ON "HEPATITIS C VIRUS"+PFT/CT

L12 15162 SEA FILE=HCAPLUS ABB=ON PLU=ON (HCV OR H(1A)C(1A)V OR HEPATITIS C VIRUS?)/OBI,BI

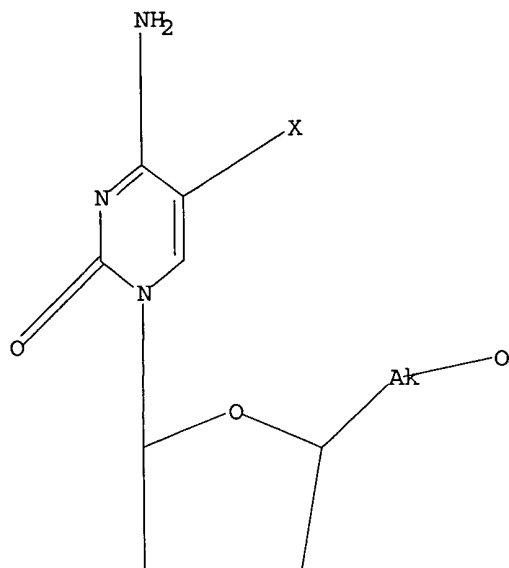
L13 90130 SEA FILE=HCAPLUS ABB=ON PLU=ON ((VIRAL?)/OBI,BI

L14 55395 SEA FILE=HCAPLUS ABB=ON PLU=ON (ANTIVIRAL?)/OBI,BI

L16 247 SEA FILE=HCAPLUS ABB=ON PLU=ON L9 AND (L10 OR L11 OR L12)

L17 53 SEA FILE=HCAPLUS ABB=ON PLU=ON L16 NOT (PY>2002 OR AY>2002 OR PRY>2002)

L20 STR



Structure attributes must be viewed using STN Express query preparation.

L22 779 SEA FILE=REGISTRY SUB=L4 SSS FUL L20
L23 279 SEA FILE=CAPLUS ABB=ON PLU=ON L22 (L) (PAC OR THU OR BAC OR
PKT OR DMA)/RL
L24 20 SEA FILE=HCAPLUS ABB=ON PLU=ON L23 AND (L10 OR L11 OR L12)
L27 168 SEA FILE=HCAPLUS ABB=ON PLU=ON L23 AND (L10 OR L11 OR L12 OR
L13 OR L14)
L30 59 SEA FILE=HCAPLUS ABB=ON PLU=ON L27 AND (HEPATITIS? OR HCV?
OR H(1A)C(1A)V?)
L33 20 SEA FILE=HCAPLUS ABB=ON PLU=ON L30 AND L24
L34 59 SEA FILE=HCAPLUS ABB=ON PLU=ON (L30 OR L33)
L35 52 SEA FILE=HCAPLUS ABB=ON PLU=ON L17 NOT L34
L36 51 SEA FILE=HCAPLUS ABB=ON PLU=ON L35 AND (HEPATITIS? OR HCV?
OR H(1A)C(1A)V?)

=> d ibib abs hitind hitstr l36 31-51

L36 ANSWER 31 OF 51 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:621109 HCAPLUS

DOCUMENT NUMBER: 129:239915

TITLE: Metabolically stabilized oxyalkylene esters and
therapeutic uses thereof

INVENTOR(S): Nudelman, Abraham; Rephaeli, Ada; Neiss, Edward; Loev,
Bernard

PATENT ASSIGNEE(S): Beacon Laboratories L.L.C., USA

SOURCE: PCT Int. Appl., 57 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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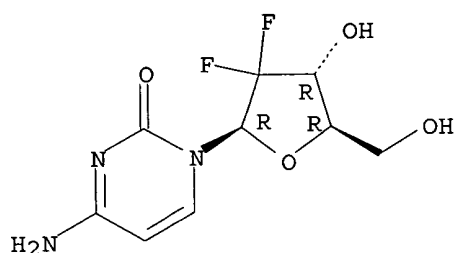
08/25/2006

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(metabolically stabilized oxyalkylene esters and therapeutic uses
thereof)

RN 95058-81-4 HCAPLUS

CN Cytidine, 2'-deoxy-2',2'-difluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 32 OF 51 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:621108 HCAPLUS

DOCUMENT NUMBER: 129:239914

TITLE: Hydroxy- and ether-containing oxyalkylene esters and
therapeutic uses thereof

INVENTOR(S): Nudelman, Abraham; Rephaeli, Adi

PATENT ASSIGNEE(S): Beacon Laboratories, L.L.C., USA

SOURCE: PCT Int. Appl., 57 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9840065	A1	19980917	WO 1998-US4764	19980311
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
US 6043389	A	20000328	US 1997-814224	19970311
CA 2283173	AA	19980917	CA 1998-2283173	19980311
AU 9865501	A1	19980929	AU 1998-65501	19980311
AU 728419	B2	20010111		
EP 998278	A1	20000510	EP 1998-911574	19980311
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
JP 2001514664	T2	20010911	JP 1998-539760	19980311
US 6239176	B1	20010529	US 2000-504786	20000215
PRIORITY APPLN. INFO.:			US 1997-814224	A 19970311

WO 1998-US4764

W 19980311

OTHER SOURCE(S): MARPAT 129:239914

AB This invention relates to compns. for and methods of treating, preventing or ameliorating cancer and other proliferative diseases as well as methods of inducing wound healing, treating cutaneous ulcers, treating gastrointestinal disorders, treating blood disorders such as anemias, immunomodulation, enhancing recombinant gene expression, treating insulin-dependent patients, treating cystic fibrosis patients, inhibiting telomerase activity, treating virus-associated tumors, especially

EBV-associated

tumors, augmenting expression of tumor suppressor genes, inducing tolerance to antigens, or treating, preventing or ameliorating protozoan infection or inhibiting histone deacetylase in cells. The compns. of the invention are to and the methods of the invention use hydroxy and ether-containing oxyalkylene esters.

IC ICM A61K031-22

ICS A61K031-235; C07C069-02; C07C069-612

CC 1-12 (Pharmacology)

Section cross-reference(s): 23, 63

IT **Hepatitis B virus**

Hepatitis C virus

Human herpesvirus 4

(tumor associated with; hydroxy- and ether-containing oxyalkylene esters and therapeutic uses thereof)

IT 120-73-0D, Purine, analogs 289-95-2D, Pyrimidine, analogs 645-05-6, Hexamethylmelamine 671-16-9, Procarbazine 4342-03-4, Dacarbazine 9015-68-3, L-Asparaginase 10540-29-1, Tamoxifen 13010-20-3D, Nitrosourea, derivs. 23214-92-8, Doxorubicin 25322-68-3D, derivs. 25322-69-4D, derivs. 51264-14-3, Amsacrine 59277-89-3, Acyclovir 65271-80-9, Mitoxantrone 82410-32-0, Ganciclovir 87940-72-5, Sarcolectin **95058-81-4**, Gemcitabine 104227-87-4, Famciclovir 213262-73-8 213262-74-9

RL: **BAC (Biological activity or effector, except adverse)**; BSU

(Biological study, unclassified); **THU (Therapeutic use)**; BIOL

(Biological study); USES (Uses)

(hydroxy- and ether-containing oxyalkylene esters and therapeutic uses thereof)

IT **95058-81-4**, Gemcitabine

RL: **BAC (Biological activity or effector, except adverse)**; BSU

(Biological study, unclassified); **THU (Therapeutic use)**; BIOL

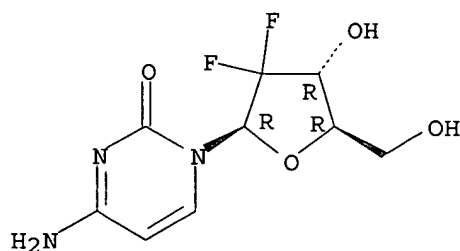
(Biological study); USES (Uses)

(hydroxy- and ether-containing oxyalkylene esters and therapeutic uses thereof)

RN 95058-81-4 HCAPLUS

CN Cytidine, 2'-deoxy-2',2'-difluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 33 OF 51 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1998:621086 HCAPLUS
 DOCUMENT NUMBER: 129:239911
 TITLE: Nitrogen-containing oxyalkylene esters and therapeutic uses thereof
 INVENTOR(S): Nudelman, Abraham; Rephaeli, Ada
 PATENT ASSIGNEE(S): Beacon Laboratories, L.L.C., USA
 SOURCE: PCT Int. Appl., 96 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9839966	A1	19980917	WO 1998-US4763	19980311
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6110970	A	20000829	US 1997-814225	19970311
AU 9865500	A1	19980929	AU 1998-65500	19980311
EP 973389	A1	20000126	EP 1998-911573	19980311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRIORITY APPLN. INFO.:			US 1997-814225	A 19970311
			WO 1998-US4763	W 19980311

OTHER SOURCE(S): MARPAT 129:239911

AB Comps. and methods are provided for treating, preventing or ameliorating cancer and other proliferative diseases, as are methods of inducing wound healing, treating cutaneous ulcers, treating gastrointestinal disorders, treating blood disorders such as anemias, immunomodulation, enhancing recombinant gene expression, treating insulin-dependent patients, treating cystic fibrosis patients, inhibiting telomerase activity, treating virus-associated tumors, especially EBV-associated tumors, modulating gene expression

and particularly augmenting expression of tumor suppressor genes, inducing tolerance to antigens, treating, preventing or ameliorating protozoan infection or inhibiting histone deacetylase in cells. The comps. of the invention are to and the methods of the invention use nitrogen-containing oxyalkyl esters.

IC ICM A01N037-10

ICS A01N055-02; C07C229-00; C07D211-78

CC 1-12 (Pharmacology)

Section cross-reference(s): 23, 25, 27, 63

IT **Hepatitis B virus**

Hepatitis C virus

Human herpesvirus 4

(tumor associated with; nitrogen-containing oxyalkylene esters and therapeutic use)

IT 107-92-6, Butyric acid, biological studies 120-73-0D, Purine, analogs
289-95-2D, Pyrimidine, analogs 645-05-6, Hexamethylmelamine 671-16-9,
Procarbazine 4342-03-4, Dacarbazine 9015-68-3, L-Asparaginase
10540-29-1, Tamoxifen 13010-20-3D, Nitrosourea, derivs. 23214-92-8,
Doxorubicin 51264-14-3, Amsacrine 59277-89-3, Acyclovir 65271-80-9,
Mitoxantrone 82410-32-0, Ganciclovir 87940-72-5, Sarcolectin
95058-81-4, Gemcitabine 104227-87-4, Famciclovir 213250-15-8
213250-17-0 213250-19-2 213250-21-6 213250-22-7 213250-23-8
213250-24-9 213250-25-0

RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); USES (Uses)
(nitrogen-containing oxyalkylene esters and therapeutic use)

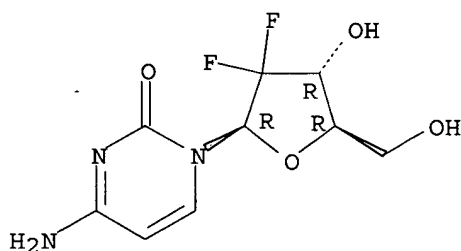
IT **95058-81-4**, Gemcitabine

RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); USES (Uses)
(nitrogen-containing oxyalkylene esters and therapeutic use)

RN 95058-81-4 HCAPLUS

CN Cytidine, 2'-deoxy-2',2'-difluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 34 OF 51 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:527193 HCAPLUS

DOCUMENT NUMBER: 129:166193

TITLE: Therapeutic treatment and prevention of infections
with a bioactive material encapsulated within a
biodegradable-biocompatible polymeric matrix

INVENTOR(S): Setterstrom, Jean A.; Van Hamont, John E.; Reid,
Robert H.; Jacob, Elliot; Jeyanthi, Ramasubbu;
Boedeker, Edgar C.; McQueen, Charles E.; Tice, Thomas
R.; Roberts, F. Donald; Friden, Phil

PATENT ASSIGNEE(S): United States Dept. of the Army, USA; Van Hamont, John
E.; et al.

SOURCE: PCT Int. Appl., 363 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 17

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9832427	A1	19980730	WO 1998-US1556	19980127

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
 DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ,
 LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
 PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US,
 UZ, VN, YU, ZW
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,
 FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,
 GA, GN, ML, MR, NE, SN, TD, TG

US 6309669	B1	20011030	US 1997-789734	19970127
AU 9863175	A1	19980818	AU 1998-63175	19980127

PRIORITY APPLN. INFO.:

US 1997-789734	A	19970127
US 1984-590308	B1	19840316
US 1992-867301	A2	19920410
US 1995-446148	A2	19950522
US 1995-446149	B2	19950522
US 1996-590973	B2	19960124
WO 1998-US1556	W	19980127

AB Novel burst-free, sustained release biocompatible and biodegradable microcapsules are disclosed which can be programmed to release their active core for variable durations ranging from 1-100 days in an aqueous physiol. environment. The microcapsules are comprised of a core of polypeptide or other biol. active agent encapsulated in a matrix of poly(lactide/glycolide) copolymer, which may contain a pharmaceutically acceptable adjuvant, as a blend of upcapped free carboxyl end group and end-capped forms ranging in ratios from 100/0 to 1/99.

IC ICM A61K009-52
 ICS A61K047-30

CC 63-5 (Pharmaceuticals)
 Section cross-reference(s): 1, 2, 15

IT **Hepatitis**
 (B, chronic; prevention of infections with bioactive material encapsulated within biodegradable-biocompatible polymeric matrix)

IT **Hepatitis**
 (C, chronic; prevention of infections with bioactive material encapsulated within biodegradable-biocompatible polymeric matrix)

IT Antigens
 RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (**hepatitis** B surface; prevention of infections with bioactive material encapsulated within biodegradable-biocompatible polymeric matrix)

IT AIDS (disease)
 Acinetobacter
 Actinomycetales
 Adenoviridae
 Adrenoceptor agonists
 Aerococcus
 Aeromonas
 Allergy inhibitors
 Alzheimer's disease
 Analgesics
 Anesthetics
 Angiogenesis
 Angiogenesis inhibitors
 Anthelmintics
 Anti-infective agents
 Anti-inflammatory agents
 Antiarrhythmics
 Antiarthritics

Antibacterial agents
Antibiotics
Anticholesteremic agents
Anticoagulants
Anticonvulsants
Antidepressants
Antidiabetic agents
Antidiarrheals
Antiemetics
Antihistamines
Antihypertensives
Antimalarials
Antimigraine agents
Antiparkinsonian agents
Antipyretics
Antirheumatic agents
Antiserums
Antitumor agents
Antitussives
Antiulcer agents
Antiviral agents
Appetite depressants
Arbovirus
Arcanobacterium haemolyticum
Arenavirus
Asthma
Bacillus (bacterium genus)
Biocompatibility
Blood substitutes
Bordetella
Borrelia
Bronchodilators
Brucella
Cachexia
Calymatobacterium
Campylobacter
Cardiopulmonary bypass
Cardiotonics
Cardiovascular agents
Cholinergic agonists
Clostridium
Contraceptives
Coronavirus
Corynebacterium
Cryptosporidium parvum
Cystic fibrosis
Cytomegalovirus
Cytotoxic agents
Decongestants
Diagnosis
Diarrhea
Dissolution rate
Diuretics
Drug bioavailability
Drug dependence
Ebola virus
Echinococcus
Electrolytes, biological
Emulsifying agents

Enterobacteriaceae
Enterococcus
Enterovirus
Epitopes
Erysipelothrix
Expectorants
Filovirus
Flavobacterium
Freeze drying
Fungicides
Gardnerella
Gram-negative bacteria
Gram-positive bacteria (Firmicutes)
Haemophilus
Haemophilus ducreyi
Helicobacter
 Hepatitis A virus
 Hepatitis B virus
 Hepatitis C virus
Human herpesvirus 3
Human herpesvirus 4
Human immunodeficiency virus
Human immunodeficiency virus 1
Human parainfluenza virus
Human poliovirus
Hypercholesterolemia
Hypnotics and Sedatives
Immunization
Immunomodulators
Immunostimulants
Infection
Influenza virus
Kidney, disease
Lactococcus
Legionella
Leptospira
Leuconostoc
Listeria
Measles virus
Melanoma
Micrococcus
Molluscum contagiosum virus
Moraxella
Multiple sclerosis
Mumps virus
Muscle relaxants
Narcotics
Neisseria
Nervous system agents
Nutrients
Opioid antagonists
Osteoarthritis
Osteomyelitis
Osteoporosis
Ovary, neoplasm
Pancreas, neoplasm
Papillomavirus
Parasitocides
Parkinson's disease

Pediococcus
Planococcus (bacterium)
Plesiomonas
Pneumonia
Poxviridae
Pseudomonas
Psoriasis
Psychotropics
Rabies virus
Reoviridae
Respiratory syncytial virus
Rheumatoid arthritis
Rhinovirus
Rhodococcus
Rotavirus
Rothia (bacterium)
Rubella virus
Salmonella typhi
Sexually transmitted diseases
Shigella boydii
Shigella dysenteriae
Shigella flexneri
Shigella sonnei
Spirillum
Staphylococcus
Streptobacillus
Streptococcus
Thrombosis
Tranquilizers
Treponema
Vaccines
Vasodilators
Vibrio
Vibrio cholerae
Wolinella succinogenes
Yersinia

(prevention of infections with bioactive material encapsulated within biodegradable-biocompatible polymeric matrix)

IT 50-06-6, Phenobarbital, biological studies 50-12-4, Mephenytoin
50-18-0, Cyclophosphamide 50-23-7, Hydrocortisone 50-24-8,
Prednisolone 50-28-2, 17 β -Estradiol, biological studies 50-33-9,
Phenylbutazone, biological studies 50-52-2, Thioridazine 50-55-5,
Reserpine 50-78-2, Aspirin 51-55-8, Atropine, biological studies
52-24-4, Thiotepe 52-76-6, Lynestrenol 53-03-2, Prednisone 53-16-7,
Estrone, biological studies 53-86-1, Indomethacin 54-11-5, Nicotine
55-48-1, Atropine sulfate 55-63-0, Nitroglycerin 55-86-7, Nitrogen
mustard 56-53-1, Diethyl stilbestrol 56-75-7, Chloramphenicol
57-27-2, Morphine, biological studies 57-33-0, Sodium pentobarbital
57-42-1, Meperidine 57-53-4, Meprobamate 57-63-6, Ethinyl estradiol
57-85-2, Testosterone propionate 57-92-1, Streptomycin a, biological
studies 58-08-2, Caffeine, biological studies 58-14-0, Pyrimethamine
58-22-0 58-25-3, Chlordiazepoxide 58-39-9, Perphenazine 58-73-1,
Diphenhydramine 59-01-8, Kanamycin a 59-05-2, Methotrexate 59-92-7,
L-Dopa, biological studies 61-33-6, Penicillin g, biological studies
67-20-9, Nitrofurantoin 68-22-4, Norethisterone 68-23-5, Norethynodrel
69-09-0, Chlorpromazine hydrochloride 69-53-4, Ampicillin 69-72-7D,
Salicylic acid, derivs. 71-58-9, Medroxyprogesterone acetate 72-33-3,
Mestranol 76-57-3, Codeine 79-57-2, Oxytetracycline 79-64-1,
Dimethisterone 91-81-6, Tripeleminamine 103-90-2, Acetaminophen

113-15-5, Ergotamine 114-07-8, Erythromycin 114-49-8, Hyoscyne hydrobromide 121-54-0 122-09-8, Phentermine 125-29-1, Dihydrocodeinone 125-71-3, Dextromethorphan 127-48-0, Trimethadione 128-62-1, Noscapine 145-94-8, Chlorindanol 148-82-3, Melphalan 155-41-9, Methscopolamine bromide 288-32-4D, Imidazole, derivs. 297-76-7, Ethynodiol diacetate 302-22-7, Chlormadinone acetate 305-03-3, Chlorambucil 309-43-3, Sodium secobarbital 315-30-0, Allopurinol 434-03-7, Ethisterone 439-14-5, Diazepam 443-48-1, Metronidazole 469-62-5 471-34-1, Calcium carbonate, biological studies 497-19-8, Sodium carbonate, biological studies 523-87-5, Dimenhydrinate 546-93-0, Magnesium carbonate 578-66-5D, 8-Aminoquinoline, derivs. 578-68-7D, 4-Aminoquinoline, derivs. 595-33-5, Megestrol acetate 738-70-5, Trimethoprim 846-50-4, Temazepam 1397-89-3, Amphotericin b 1397-94-0, Antimycin a 1403-66-3, Gentamicin 1404-26-8, Polymyxin b 1404-90-6, Vancomycin 1406-05-9D, Penicillin, derivs. 4696-76-8, Kanamycin b 5588-33-0, Mesoridazine 5633-18-1, Melengestrol 5786-21-0, Clozapine 5800-19-1, Metiapine 6533-00-2, Norgestrel 7447-40-7, Potassium chloride (KCl), biological studies 8063-07-8, Kanamycin 9000-83-3, Atpase 9000-92-4, Amylase 9001-62-1, Lipase 9001-63-2, Muramidase 9001-67-6, Neuraminidase 9001-78-9, Alkaline phosphatase 9001-99-4, Ribonuclease 9002-02-2, Succinic acid dehydrogenase 9002-07-7, Trypsin 9004-07-3, Chymotrypsin 9004-10-8, Insulin, biological studies 9025-82-5, Phosphodiesterase 9029-12-3, Glutamic acid dehydrogenase 9035-74-9, Glycogen phosphorylase 9046-27-9, γ -Glutamyltranspeptidase 9079-67-8 10118-90-8, Minocycline 11111-12-9, Cephalosporins 13292-46-1, Rifampin 14271-04-6 21645-51-2, Aluminum hydroxide, biological studies 22232-71-9, Mazindol 24730-10-7, Dihydroergocristine methanesulfonate 25447-66-9 26780-50-7, Poly(lactide co-glycolide) 26787-78-0, Amoxicillin 30516-87-1, Azt 32986-56-4, Tobramycin 35189-28-7, Norgestimate 37205-61-1, Proteinase inhibitor 37517-28-5, Amikacin 53678-77-6D, Muramyl dipeptide, derivs. 53994-73-3, Cefaclor 55268-75-2, Cefuroxime 61036-62-2, Teicoplanin 64221-86-9, Imipenem 80738-43-8, Lincosamide 81103-11-9, Clarithromycin 82419-36-1, Ofloxacin 85721-33-1, Ciprofloxacin

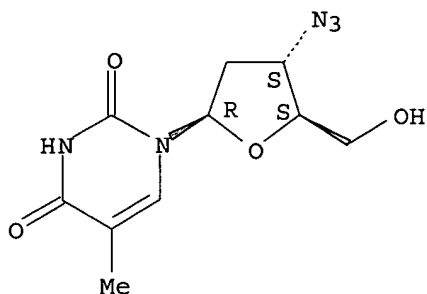
RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(prevention of infections with bioactive material encapsulated within biodegradable-biocompatible polymeric matrix)

IT 30516-87-1, Azt
RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(prevention of infections with bioactive material encapsulated within biodegradable-biocompatible polymeric matrix)

RN 30516-87-1 HCAPLUS

CN Thymidine, 3'-azido-3'-deoxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 35 OF 51 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:484946 HCAPLUS

DOCUMENT NUMBER: 129:121659

TITLE: A method of modulating an immune response in an infected mammal by transmucosal administration of modulating agent

INVENTOR(S): Michaels, Frank; Block, Timothy

PATENT ASSIGNEE(S): Thomas Jefferson University, USA

SOURCE: PCT Int. Appl., 55 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9829121	A1	19980709	WO 1998-US4116	19980102
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2276450	AA	19980709	CA 1998-2276450	19980102
EP 979080	A1	20000216	EP 1998-911458	19980102
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001507360	T2	20010605	JP 1998-530372	19980102
US 6355248	B1	20020312	US 1999-334819	19990617
PRIORITY APPLN. INFO.:			US 1997-34596P	P 19970102
			WO 1998-US4116	W 19980102

AB Methods and compns. for modulating an immune response in mammals infected with a bacterium, a virus, or a parasite are provided. The methods and compns. are useful in mammals experiencing acute or chronic infections. The methods and compns. may be used in conjunction with known treatments for infection. The method entails the transmucosal administration of a composition comprising and epitope. The epitope of the mol. administered may be an epitope located on an antigen of the infectious agent or and epitope located on a tissue of the mammal. Typically, the tissue-derived epitope becomes reactive with the immune system and produces adverse or undesirable effects after the mammal is infected.

IC ICM A61K031-505

ICS A61K031-52; A61K031-655; A61K031-557; A61K035-12; A61K035-66; C07H019-073; C07H019-173

CC 15-10 (Immunochemistry)

Section cross-reference(s): 1

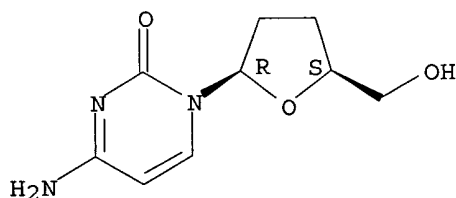
IT B19 virus
Borna disease virus
Hepatitis B virus
Hepatitis C virus
Human T-lymphotropic virus 1
Human immunodeficiency virus
Leishmania donovani
Mycobacterium tuberculosis
Onchocerca volvulus
Schistosoma mansoni
Streptococcus group B
Streptococcus mutans
Trypanosoma cruzi
(method of modulating an immune response in an infected mammal by transmucosal administration of epitopes and anti-infectious agents in relation to)

IT 7481-89-2, Ddc 30516-87-1, Azt 59865-13-3, Cyclosporin
A 69655-05-6, Ddi 134678-17-4, 3Tc
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); USES (Uses)
(method of modulating an immune response in an infected mammal by transmucosal administration of epitopes and anti-infectious agents)

IT 7481-89-2, Ddc 30516-87-1, Azt
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); USES (Uses)
(method of modulating an immune response in an infected mammal by transmucosal administration of epitopes and anti-infectious agents)

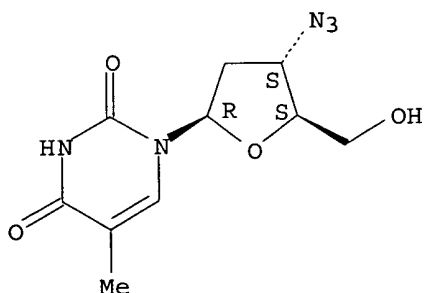
RN 7481-89-2 HCAPLUS
CN Cytidine, 2',3'-dideoxy- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 30516-87-1 HCAPLUS
CN Thymidine, 3'-azido-3'-deoxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 36 OF 51 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:484940 HCAPLUS

DOCUMENT NUMBER: 129:104235

TITLE: Tricarboxylic acid-containing oxyalkyl esters, and therapeutic uses thereof

INVENTOR(S): Nudelman, Abraham; Rephaeli, Ada

PATENT ASSIGNEE(S): Beacon Laboratories L.L.C., USA

SOURCE: PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9829114	A1	19980709	WO 1997-US23725	19971230
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
-US 6130248	A	20001010	US 1996-781905	19961230
AU 9856173	A1	19980731	AU 1998-56173	19971230
EP 961614	A1	19991208	EP 1997-952599	19971230
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
PRIORITY APPLN. INFO.:			US 1996-781905	A 19961230
			US 1997-814365	A 19970311
			WO 1997-US23725	W 19971230

OTHER SOURCE(S): MARPAT 129:104235

AB Comps. for and methods of treating, preventing or ameliorating cancer and other proliferative diseases are provided, as are methods of inducing wound healing, treating cutaneous ulcers, treating gastrointestinal disorders, treating blood disorders such as anemias, immunomodulation, enhancing recombinant gene expression, treating insulin-dependent patients, treating cystic fibrosis patients, inhibiting telomerase activity, treating virus-associated tumors, especially EBV-associated tumors, modulating gene expression and particularly augmenting expression of tumor suppressor genes, inducing tolerance to antigens; treating, preventing, or ameliorating protozoan infection or inhibiting histone deacetylase in cells. The methods of the invention use tricarboxylic acid substituted oxyalkyl esters.

IC ICM A61K031-225

ICS C07C069-612; C07C069-67

CC 1-12 (Pharmacology)

Section cross-reference(s): 23

IT **Hepatitis B virus**

Hepatitis C virus

Human herpesvirus 4

(tumor associated with; tricarboxylic acid-containing oxyalkyl esters, and therapeutic uses thereof)

IT 120-73-0D, Purine, analogs 289-95-2D, Pyrimidine, analogs 645-05-6,

Hexamethylmelamine 671-16-9, Procarbazine 4342-03-4, Dacarbazine 9015-68-3, L-Asparaginase 10540-29-1, Tamoxifen 13010-20-3D, Nitrosourea, derivs. 23214-92-8, Doxorubicin 33419-42-0 51264-14-3, Amsacrine 59277-89-3, Acyclovir 65271-80-9, Mitoxantrone 82410-32-0, Ganciclovir 95058-81-4, Gemcitabine 104227-87-4, Famciclovir 210107-02-1 210107-03-2

RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(tricarboxylic acid-containing oxyalkyl esters, and therapeutic uses thereof)

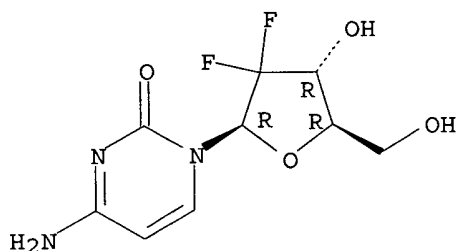
IT 95058-81-4, Gemcitabine

RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(tricarboxylic acid-containing oxyalkyl esters, and therapeutic uses thereof)

RN 95058-81-4 HCAPLUS

CN Cytidine, 2'-deoxy-2',2'-difluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 37 OF 51 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:268361 HCAPLUS

DOCUMENT NUMBER: 128:317245

TITLE: Methods of using sucrose octasulfate to treat or prevent enveloped virus infection

INVENTOR(S): Navia, Manuel A.

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Inc., USA

SOURCE: PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9817282	A1	19980430	WO 1997-US19181	19971023
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,			

1. *Chrysomelids* (1000 spp.)

AB Sucrose octasulfate and its pharmaceutically acceptable salts, including sucralfate (basic Al salt of sucrose octasulfate), alone or in combination with other agents, are useful in topical compns. and methods for treating or preventing viral infections, especially infections caused by enveloped viruses such as HIV and herpesvirus. Sucralfate is an extremely safe drug, tolerated at ≥ 1 g/kg in animal studies. Thus, sucrose octasulfate inhibited HIV-1-18a replication in peripheral blood mononuclear cells in vitro with $IC_{50} = 0.03$ mg/mL, and inhibited replication of the cells with $IC_{50} > 25.0$ mg/mL.

IT Animal virus

Blood

Blood plasma

Body fluid

Coating materials

Cytomegalovirus

Dengue virus

Dental materials and appliances

Disinfectants

Egg

Epithelium

Feed

Flaviviridae

Hepadnaviridae

Hepatitis B virus

Hepatitis C virus

Herpesviridae

Human herpesvirus 1

Human herpesvirus 2

Human herpesvirus 3

Human herpesvirus 4

Human immunodeficiency virus 1

Human immunodeficiency virus 2

Influenza A virus

Influenza B virus

Influenza C virus

Laboratory ware

Mumps virus

Orthomyxoviridae

Paramyxoviridae

Rabies virus

Respiratory syncytial virus

Retroviridae

Rhabdoviridae

Semen

(methods of using sucrose octasulfate to treat or prevent enveloped virus infection)

IT 30516-87-1 54182-58-0, Sucralfate 57680-56-5, Sucrose
octasulfate 73264-44-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(methods of using sucrose octasulfate to treat or prevent enveloped virus infection)

IT 30516-87-1

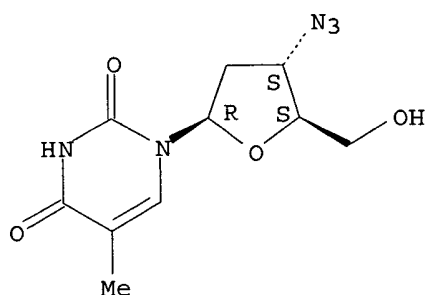
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(methods of using sucrose octasulfate to treat or prevent enveloped virus infection)

RN 30516-87-1 HCAPLUS

CN Thymidine, 3'-azido-3'-deoxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 38 OF 51 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:223587 HCAPLUS

DOCUMENT NUMBER: 129:13861

TITLE: Inhibition of the *hepatitis C virus* helicase-associated ATPase activity by the combination of ADP, NaF, MgCl₂, and poly(rU). Two ADP binding sites on the enzyme-nucleic acid complex
AUTHOR(S): Porter, David J. T.
CORPORATE SOURCE: Glaxo Wellcome, Research Triangle Park, NC, 27709, USA
SOURCE: Journal of Biological Chemistry (1998), 273(13), 7390-7396

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Hepatitis C virus (HCV) helicase** has an intrinsic ATPase activity and a nucleic acid (poly(rU))-stimulated ATPase activity. The poly(rU)-stimulated ATPase activity was inhibited by F⁻ in a time-dependent manner during ATP hydrolysis. Inhibition was the result of trapping an enzyme-bound ADP-poly(rU) ternary complex generated during the catalytic cycle and was not the result of generating enzyme-free ADP that subsequently inhibited the enzyme. However, catalysis was not required for efficient inhibition by F⁻. The stimulated and the intrinsic ATPase activities were also inhibited by treatment of the enzyme with F⁻, ADP, and poly(rU). The inhibited enzyme slowly recovered (t_{1/2} = 23 min) ATPase activity after a 2000-fold dilution into assay buffer. The onset of inhibition by 500 μM ADP and 15 mM F⁻ in the absence of nucleic acid was very slow (t_{1/2} >40 min). However, the sequence of addition of poly(rU) to a diluted solution of ADP/NaF-treated enzyme

had a profound effect on the extent of inhibition. If the ADP/NaF-treated enzyme was diluted into an assay that lacked poly(rU) and the assay was subsequently initiated with poly(rU), the treated enzyme was not inhibited. Alternatively, if the treated enzyme was diluted into an assay containing poly(rU), the enzyme was inhibited. ATP protected the enzyme from inhibition by ADP/NaF. The stoichiometry between ADP and enzyme monomer in the inhibited enzyme complex was 2, as determined from titration of the

ATPase

activity ($[ADP]/[E] = 2.2$) and from the number of radiolabeled ADP bound to the inhibited enzyme ($[ADP]/[E] = 1.7$) in the presence of excess NaF, MgCl₂, and poly(rU). The Hill coefficient for titration of ATPase activity

with

F⁻ (.8) or MgCl₂ (.1) in the presence of excess ADP and poly(rU) suggested that multiple F⁻ and Mg²⁺ were involved in forming the inhibited enzyme complex. The stoichiometry between (dU)₁₈, a defined oligomeric nucleic acid substituting for poly(rU), and enzyme monomer in the inhibited enzyme complex was estimated to be 1 ($[(dU)_{18}/E] = 1.2$) from titration of the ATPase activity in the presence of excess ADP, MgCl₂, and NaF.

CC 7-4 (Enzymes)

ST **hepatitis C virus** helicase ATPase

IT Enzymes, biological studies

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(RNA-unwinding, helicases; inhibition of the **hepatitis C virus** helicase-associated ATPase activity)

IT **Hepatitis C virus**

(inhibition of the **hepatitis C virus** helicase-associated ATPase activity)

IT 9000-83-3, ATPase

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(inhibition of the **hepatitis C virus** helicase-associated ATPase activity)

IT 58-64-0, 5'-ADP, biological studies 7681-49-4, Sodium fluoride (NaF), biological studies 7786-30-3, Magnesium chloride (MgCl₂), biological studies 27416-86-0, Poly(rU)

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(inhibition of the **hepatitis C virus** helicase-associated ATPase activity)

IT 27416-86-0, Poly(rU)

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(inhibition of the **hepatitis C virus** helicase-associated ATPase activity)

RN 27416-86-0 HCAPLUS

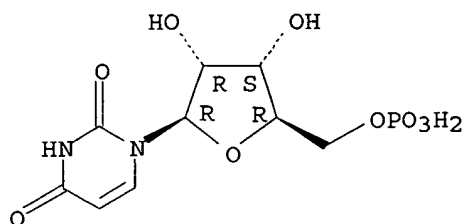
CN 5'-Uridylic acid, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 58-97-9

CMF C9 H13 N2 O9 P

Absolute stereochemistry.



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 39 OF 51 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:41720 HCAPLUS

DOCUMENT NUMBER: 128:110885

TITLE: Succinamic acid and succinimide derivatives having anti-inflammatory, anti-viral, and bronchodilating activity, preparation, compositions, and combinations with reverse transcriptase inhibitors

INVENTOR(S): Hamed-Sangsari, Farid; Nugier, Fabienne; Vallet, Thierry; Grange, Jacques; Vila, Jorge

PATENT ASSIGNEE(S): Compagnie De Developpement Aguettant S.A., Fr.

SOURCE: U.S., 26 pp., Cont.-in-part of U.S. Ser. No. 528,879.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

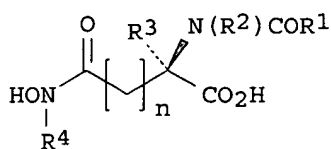
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

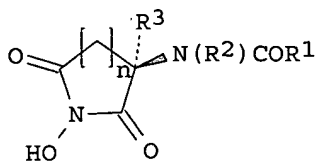
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5705522	A	19980106	US 1996-600525	19960213
CA 2231996	AA	19970320	CA 1996-2231996	19960913
WO 9710205	A1	19970320	WO 1996-IB942	19960913
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI			
AU 9668350	A1	19970401	AU 1996-68350	19960913
EP 854860	A1	19980729	EP 1996-928647	19960913
EP 854860	B1	20010725		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
JP 2000511871	T2	20000912	JP 1997-511797	19960913
AT 203513	E	20010815	AT 1996-928647	19960913
PRIORITY APPLN. INFO.:			US 1995-528879	A2 19950915
			US 1996-600525	A 19960213
			WO 1996-IB942	W 19960913

OTHER SOURCE(S): MARPAT 128:110885

GI



I



II

AB A new family of compds. are provided having anti-inflammatory, anti-viral, and bronchodilating activity. The compds are I and II [R1 = (halo-substituted) C1-4 alkyl; R2-R4 = H, (substituted) (branched) C1-8 alkyl, etc.]. Also provided are compns. of these compds., which alone, and in combination with reverse transcriptase inhibitors thereby resulting in an additive or synergistic effect, are useful in inhibiting or suppressing viruses including those exhibiting retroviral replication, or in treating viruses including a retrovirus such as HIV in a human cell population. Methods of using these compns., compds., and salts thereof are also provided. Preparation and anti-HIV activity of e.g. D-acetamido-N-hydroxysuccinamic acid are included.

IC ICM A01N043-36

ICS C07D205-10; C12P021-02; C07C209-28

INCL 514423000

CC 1-12 (Pharmacology)

IT AIDS (disease)

Antiasthmatics

Antiviral agents

Hepatitis B virus

Hepatitis C virus

Human T-lymphotropic virus 1

Human T-lymphotropic virus 2

Human herpesvirus

Human immunodeficiency virus

Human immunodeficiency virus 1

Human immunodeficiency virus 2

Retroviridae

Simian immunodeficiency virus

(succinamic acid and succinimide derivs. with antiinflammatory, antiviral, and bronchodilating activity, preparation, compns., and combinations with reverse transcriptase inhibitors)

IT 3056-17-5, d4T 3416-05-5 4097-22-7, Dideoxyadenosine

7481-89-2, DdC 30516-87-1, AZT 69655-05-6, DdI

85326-06-3 134678-17-4, 3TC 188945-89-3 188945-90-6 188945-91-7

188945-92-8

RL: **BAC (Biological activity or effector, except adverse)**; BSU

(Biological study, unclassified); **THU (Therapeutic use)**; BIOL

(Biological study); USES (Uses)

(succinamic acid and succinimide derivs. with antiinflammatory, antiviral, and bronchodilating activity, preparation, compns., and combinations with reverse transcriptase inhibitors)

IT 3416-05-5 7481-89-2, DdC 30516-87-1, AZT

RL: **BAC (Biological activity or effector, except adverse)**; BSU

(Biological study, unclassified); **THU (Therapeutic use)**; BIOL

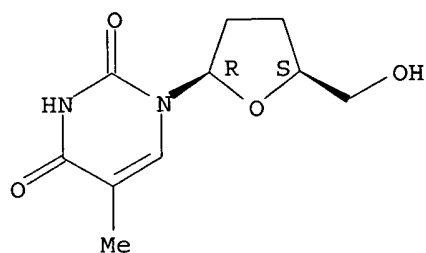
(Biological study); USES (Uses)

(succinamic acid and succinimide derivs. with antiinflammatory, antiviral, and bronchodilating activity, preparation, compns., and combinations with reverse transcriptase inhibitors)

RN 3416-05-5 HCAPLUS

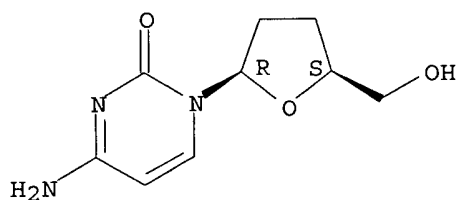
CN Thymidine, 3'-deoxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



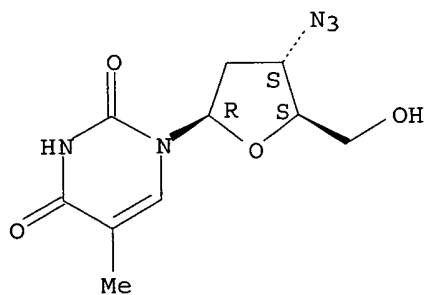
RN 7481-89-2 HCAPLUS
CN Cytidine, 2',3'-dideoxy- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 30516-87-1 HCAPLUS
CN Thymidine, 3'-azido-3'-deoxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 40 OF 51 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:470070 HCAPLUS

DOCUMENT NUMBER: 127:76006

TITLE: Compositions and methods of developing oligonucleotides and oligonucleotide analogs having antiviral activity

INVENTOR(S): Wang, Jin-Feng; Pan, Weihua

PATENT ASSIGNEE(S): Penn State Research Foundation, USA

SOURCE: PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9720072	A1	19970605	WO 1996-US18921	19961127
W: AU, CA, JP, KR				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5856085	A	19990105	US 1995-566216	19951201
AU 9711241	A1	19970619	AU 1997-11241	19961127
PRIORITY APPLN. INFO.:			US 1995-566216	A 19951201
			WO 1996-US18921	W 19961127

AB Methods of identifying and preparing nucleic acid compds. that bind to RSV and potentially have anti-viral activity are disclosed, as well as nucleic acid compns. having anti-viral activity. The methods comprise iterative binding, separating and amplifying of nucleic acids or nucleic acid analogs (SELEX) using an intact virus as the receptor mol.

IC ICM C12Q001-68

ICS C12P019-34

CC 1-5 (Pharmacology)

Section cross-reference(s): 3, 63

IT Antiviral agents

Bacteria (Eubacteria)

Combinatorial library

Cytomegalovirus

Fungi

Hepatitis A virus

Hepatitis B virus

Hepatitis C virus

Hepatitis E virus

Hepatitis delta virus

Human T-lymphotropic virus

Human herpesvirus 1

Human herpesvirus 2

Human herpesvirus 4

Human herpesvirus 6

Human herpesvirus 7

Human immunodeficiency virus

Human papillomavirus

PCR (polymerase chain reaction)

Parasite

RNA sequences

Rous sarcoma virus

Virus

Yeast

(compns. and methods of developing oligonucleotides and oligonucleotide analogs having antiviral activity)

IT 4546-70-7D, 2-Amino-2'-deoxyadenosine, derivs. **10212-20-1D**,

2'-Fluoro-2'-deoxycytidine, derivs. **26889-39-4D**,

2'-Amino-2'-deoxyuridine, derivs. 60966-26-9D, 2'-Amino-2'-

deoxyguanosine, derivs. 64183-27-3D, 2'-Fluoro-2'-deoxyadenosine,

derivs. 78842-13-4D, Guanosine, 2'-deoxy-2'-fluoro-, derivs.

RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(compns. and methods of developing oligonucleotides and oligonucleotide analogs having antiviral activity)

IT **10212-20-1D**, 2'-Fluoro-2'-deoxycytidine, derivs.

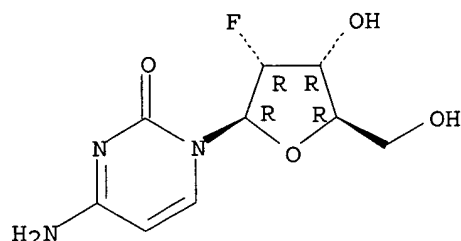
26889-39-4D, 2'-Amino-2'-deoxyuridine, derivs.

RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(comps. and methods of developing oligonucleotides and oligonucleotide
analogs having antiviral activity)

RN 10212-20-1 HCAPLUS

CN Cytidine, 2'-deoxy-2'-fluoro- (8CI, 9CI) (CA INDEX NAME)

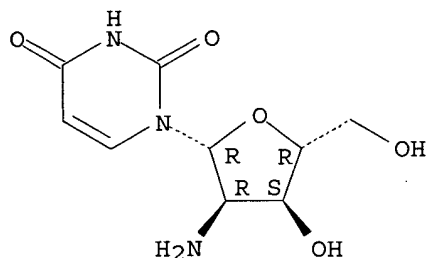
Absolute stereochemistry.



RN 26889-39-4 HCAPLUS

CN Uridine, 2'-amino-2'-deoxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L36 ANSWER 41 OF 51 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:251184 HCAPLUS

DOCUMENT NUMBER: 126:314020

TITLE: Polynucleotide modulation of the protease, nucleoside
triphosphatase, and helicase activities of a
hepatitis C virus NS3-NS4A

AUTHOR(S): complex isolated from transfected COS cells
Morgenstern, Kurt A.; Landro, James A.; Hsiao, Kathy;
Lin, Chao; Gu, Yong; Su, Michael S.-S.; Thomson, John
A.

CORPORATE SOURCE: Vertex Pharmaceuticals Incorporated, Cambridge, MA,
02139-4242, USA

SOURCE: Journal of Virology (1997), 71(5), 3767-3775
CODEN: JOVIAM; ISSN: 0022-538X

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The **hepatitis C virus** (HCV)
nonstructural 3 protein (NS3) is a 70-kDa multifunctional enzyme with
three known catalytic activities segregated in two somewhat independent
domains. The essential machinery of a serine protease is localized in the
N-terminal one-third of the protein, and nucleoside triphosphatase
(NTPase) and helicase activities reside in the remaining C-terminal

region. NS4A is a 54-residue protein expressed immediately downstream of NS3 in the viral polyprotein, and a central stretch of hydrophobic residues in NS4A form an integral structural component of the NS3 serine protease domain. There is no evidence to suggest that the two domains of NS3 are separated by proteolytic processing in vivo. This may reflect economical packaging of essential viral replicative components, but it could also mean that there is functional interdependence between the two domains. In this study, a full-length NS3-NS4A complex was isolated after expression and autoprocessing in transiently transfected COS cells. The protein was used to examine the effects of polynucleotides on the NTPase, helicase, and protease activities. Unlike the previously reported behavior of a sep. expressed NS3 helicase domain, the full NS3-NS4A complex demonstrated optimal NTPase activity between pH 7.5 and 8.5. All three NS3-NS4A activities were modulated by polynucleotides, and poly(U) having the most remarkable effect. These findings suggest that the domains within NS3 may influence the activity of one another and that the interplay of *HCV* genomic elements may regulate the enzyme activities of this complex *HCV* replicase component.

- CC 7-3 (Enzymes)
- ST nonstructural protein enzyme domain interaction virus; protein NS3 NS4 enzyme domain interaction; protease protein NS3 NS4 complex virus; helicase protein NS3 NS4 complex virus; ATPase protein NS3 NS4 complex virus; **hepatitis** virus protein NS3 NS4 interaction
- IT Proteins, specific or class
 RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
 (NS3 (nonstructural, 3), noncovalent complex with NS4 protein; polynucleotide modulation of the protease, nucleoside triphosphatase, and helicase activities of a **hepatitis C virus** NS3-NS4A complex isolated from transfected COS cells)
- IT Proteins, specific or class
 RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
 (NS4 (nonstructural, 4), noncovalent complex with NS3 protein; polynucleotide modulation of the protease, nucleoside triphosphatase, and helicase activities of a **hepatitis C virus** NS3-NS4A complex isolated from transfected COS cells)
- IT Enzymes, biological studies
 RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
 (RNA-unwinding, helicases; polynucleotide modulation of the protease, nucleoside triphosphatase, and helicase activities of a **hepatitis C virus** NS3-NS4A complex isolated from transfected COS cells)
- IT **Hepatitis C virus**
 (polynucleotide modulation of the protease, nucleoside triphosphatase, and helicase activities of a **hepatitis C virus** NS3-NS4A complex isolated from transfected COS cells)
- IT Polynucleotides
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (polynucleotide modulation of the protease, nucleoside triphosphatase, and helicase activities of a **hepatitis C virus** NS3-NS4A complex isolated from transfected COS cells)
- IT 24937-83-5, Poly (A) 25609-92-1, Poly (dC) 27416-86-0, Poly (U) 30811-80-4, Poly (C)
 RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
 (polynucleotide modulation of the protease, nucleoside triphosphatase,

and helicase activities of a *hepatitis C*

virus NS3-NS4A complex isolated from transfected COS cells)

IT 9000-83-3, ATPase 9075-51-8, Nucleoside triphosphatase 37259-58-8,
Serine proteinase

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP
(Properties); BIOL (Biological study); PROC (Process)

(polynucleotide modulation of the protease, nucleoside triphosphatase,
and helicase activities of a *hepatitis C*

virus NS3-NS4A complex isolated from transfected COS cells)

IT 25609-92-1, Poly (dC) 27416-86-0, Poly (U)
30811-80-4, Poly (C)

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); BIOL (Biological study)

(polynucleotide modulation of the protease, nucleoside triphosphatase,
and helicase activities of a *hepatitis C*

virus NS3-NS4A complex isolated from transfected COS cells)

RN 25609-92-1 HCAPLUS

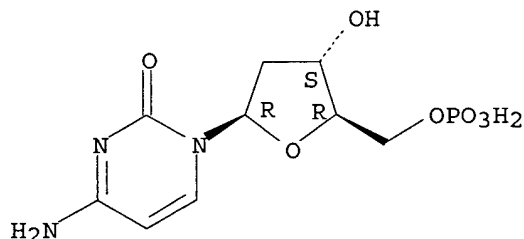
CN 5'-Cytidylic acid, 2'-deoxy-, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 1032-65-1

CMF C9 H14 N3 O7 P

Absolute stereochemistry.



RN 27416-86-0 HCAPLUS

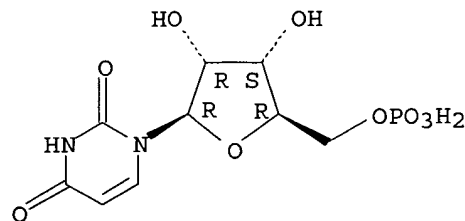
CN 5'-Uridylic acid, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 58-97-9

CMF C9 H13 N2 O9 P

Absolute stereochemistry.



RN 30811-80-4 HCAPLUS

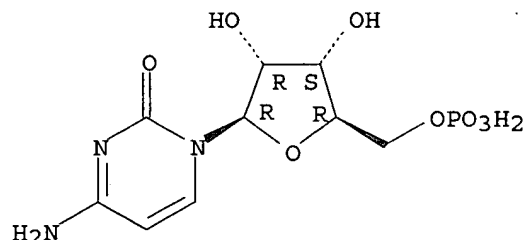
CN 5'-Cytidylic acid, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 63-37-6

CMF C9 H14 N3 O8 P

Absolute stereochemistry.



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 42 OF 51 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:145135 HCAPLUS

DOCUMENT NUMBER: 126:144506

TITLE: Preparation of phosphorothioate-linked oligodeoxyribonucleotides as virucides, antitumors, and antiinflammatory agents

INVENTOR(S): Cook, Phillip Dan; Hoke, Glenn

PATENT ASSIGNEE(S): Isis Pharmaceuticals, Inc., USA; Cook, Phillip Dan; Hoke, Glenn

SOURCE: PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 321

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9639154	A1	19961212	WO 1996-US8757	19960605
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5576302	A	19961119	US 1995-468447	19950606
US 5587361	A	19961224	US 1995-469851	19950606
US 5599797	A	19970204	US 1995-471967	19950606
US 5607923	A	19970304	US 1995-467597	19950606
US 5620963	A	19970415	US 1995-468569	19950606
US 5635488	A	19970603	US 1995-470129	19950606
US 5654284	A	19970805	US 1995-466692	19950606
US 5661134	A	19970826	US 1995-471966	19950606
AU 9662528	A1	19961224	AU 1996-62528	19960605
AU 698739	B2	19981105		
EP 831854	A1	19980401	EP 1996-921270	19960605
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, FI

JP 10510433	T2	19981013	JP 1997-501254	19960605
AU 9726244	A1	19971106	AU 1997-26244	19970624
AU 713740	B2	19991209		
NO 9705558	A	19980126	NO 1997-5558	19971202
US 6232463	B1	20010515	US 1998-128508	19980804

PRIORITY APPLN. INFO.:

	US 1995-466692	A1	19950606
	US 1995-467597	A1	19950606
	US 1995-468447	A1	19950606
	US 1995-468569	A1	19950606
	US 1995-469851	A1	19950606
	US 1995-470129	A1	19950606
	US 1995-471966	A1	19950606
	US 1995-471967	A1	19950606
	US 1991-777670	A3	19911015
	US 1991-777007	B2	19911016
	AU 1993-38025	A3	19930225
	US 1993-58023	A2	19930505
	US 1994-297703	A2	19940829
	WO 1996-US8757	W	19960605
	US 1997-948151	A1	19971009

AB Sequence-specific phosphorothioate oligodeoxyribonucleotides comprising nucleoside units which are joined together by either substantially all Sp or substantially all rp phosphorothioate inter-sugar linkages are provided. Such sequence-specific phosphorothioate oligodeoxyribonucleotides having substantially chirally pure inter-sugar linkages are prepared by enzymic or chemical preparation Title

phosphorothioate-linked oligodeoxyribonucleotides were prepared and tested (1-1000 µg/kg body weight) for treatment of **hepatitis** caused by **HCV**, inflammatory disease, C-raf kinase mediated cancer , and AIDS.

IC ICM A61K031-70
ICS C07H021-00

CC 33-9 (Carbohydrates)
Section cross-reference(s): 1, 63

IT 144245-52-3P 149594-04-7P 149957-14-2P 151879-73-1P
154719-23-0P 155752-67-3P 155752-73-1P 155752-74-2P
156657-98-6P 177075-18-2P 183451-56-1P 185229-55-4P
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phosphorothioate-linked oligodeoxyribonucleotides as virucides, antitumors, and antiinflammatory agents)

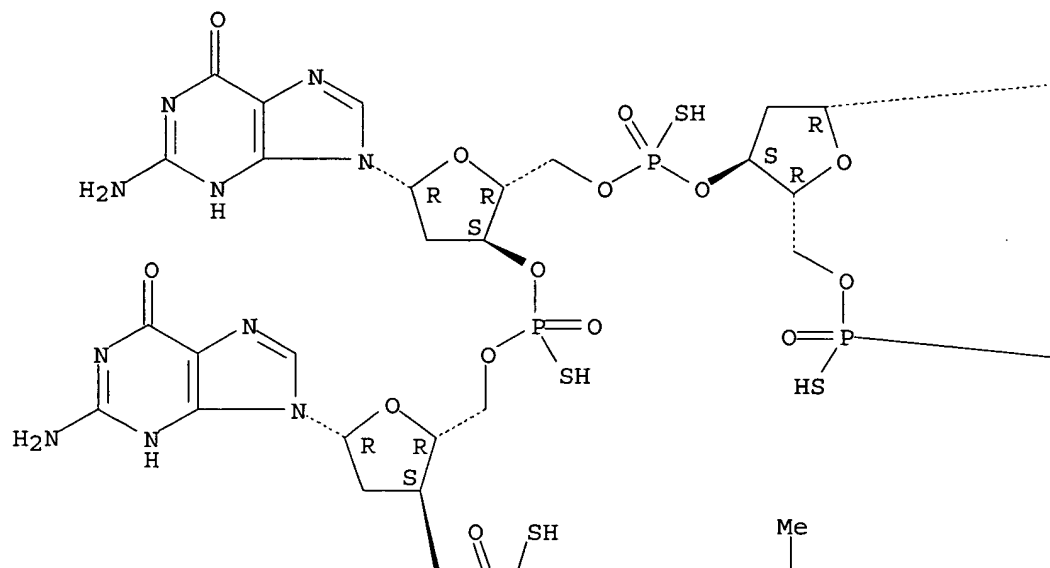
IT **154719-23-0P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phosphorothioate-linked oligodeoxyribonucleotides as virucides, antitumors, and antiinflammatory agents)

RN 154719-23-0 HCAPLUS

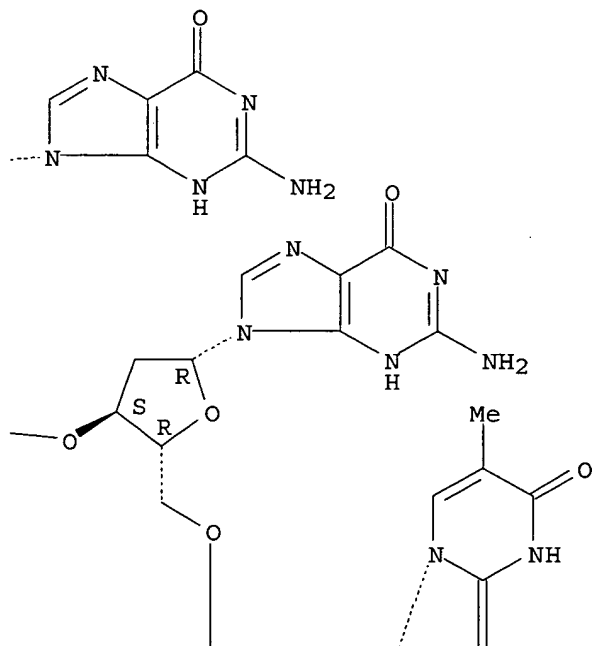
CN Thymidine, P-thiothymidylyl-(3'→5')-P-thiothymidylyl-(3'→5')-2'-deoxy-P-thioguanilyl-(3'→5')-2'-deoxy-P-thioguanilyl-(3'→5')-2'-deoxy-P-thioguanilyl-(3'→5')-P-thiothymidylyl-(3'→5')- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

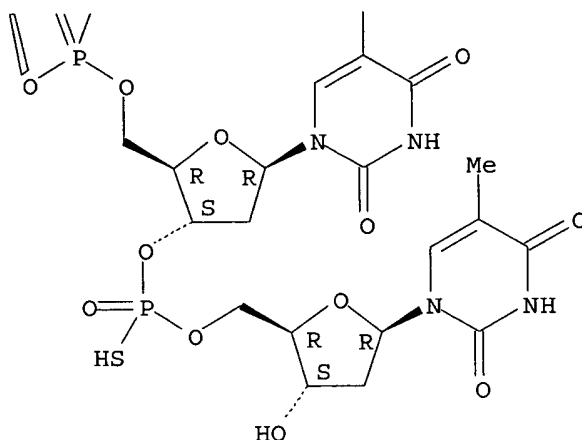
PAGE 1-A



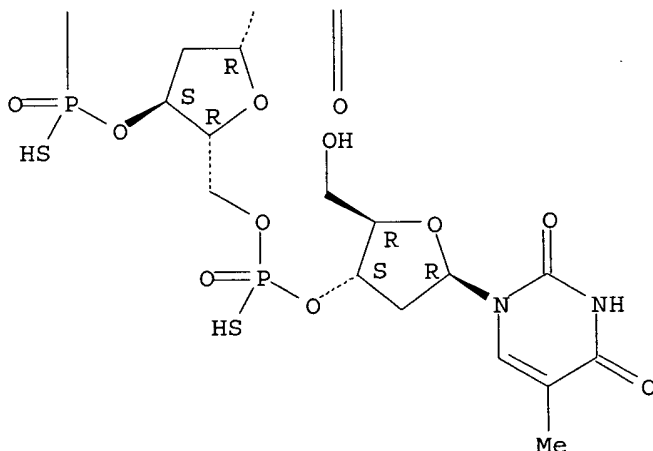
PAGE 1-B



PAGE 2-A



PAGE 2-B



L36 ANSWER 43 OF 51 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:440967 HCAPLUS

DOCUMENT NUMBER: 125:78532

TITLE: Nucleic acid detection and identification using site-specific cleavage, especially for analysis of human disease-related mutant gene or microbial pathogen nucleic acid analysis

INVENTOR(S): Dahlberg, James E.; Lyamichev, Victor I.; Brow, Mary Ann D.; Oldenburg, Mary C.; Heisler, Laura M.; Fors, Lance; Olive, David Michael

PATENT ASSIGNEE(S): Third Wave Technologies, Inc., USA

SOURCE: PCT Int. Appl., 432 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9615267	A1	19960523	WO 1995-US14673	19951109
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5843654	A	19981201	US 1995-484956	19950607
US 6372424	B1	20020416	US 1995-520946	19950830
AU 9642347	A1	19960606	AU 1996-42347	19951109
EP 788557	A1	19970813	EP 1995-940678	19951109
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10509322	T2	19980914	JP 1995-516227	19951109

PRIORITY APPLN. INFO.:

US 1994-337164	A	19941109
US 1995-402601	A	19950309
US 1995-484956	A	19950607
US 1995-520946	A2	19950830
US 1992-986330	A2	19921207
US 1993-73384	A2	19930604
US 1994-254359	A2	19940606
WO 1995-US14673	W	19951109

AB The present invention relates to means for cleaving a nucleic acid in a site-specific manner. Enzymes, including 5' nucleases and 3' exonucleases, are used to screen for known and unknown mutations, including single base changes, in nucleic acids. Methods are provided which allow for the identification of genetic mutations in human gene sequences, including the human p53 gene, in a sample. Methods are provided which allow for the detection and identification of bacterial and viral pathogens and species in a sample.

IC ICM C12Q001-68

ICS C12Q001-70; C12P019-34; C12N009-22; A61K038-47; G01N027-26; C07H021-02

CC 3-1 (Biochemical Genetics)

Section cross-reference(s): 10, 14

IT **Virus, animal**

(**hepatitis C**, gene anal.; nucleic acid detection and identification using site-specific cleavage, especially for anal. of human disease-related mutant gene or microbial pathogen nucleic acid anal.)

IT **1173-82-6**, Dutp 67460-15-5 101515-08-6, 7'-Deaza-2'-deoxyguanosine-5'-triphosphate

RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); **THU (Therapeutic use)**; ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)

(of nucleic acid analog substrate; nucleic acid detection and identification using site-specific cleavage, especially for anal. of human disease-related mutant gene or microbial pathogen nucleic acid anal.)

IT **1173-82-6**, Dutp

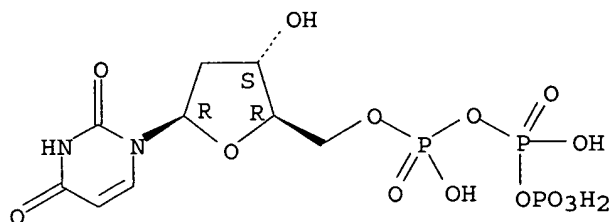
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); **THU (Therapeutic use)**; ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)

(of nucleic acid analog substrate; nucleic acid detection and identification using site-specific cleavage, especially for anal. of human disease-related mutant gene or microbial pathogen nucleic acid anal.)

RN 1173-82-6 HCAPLUS

CN Uridine 5'-(tetrahydrogen triphosphate), 2'-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L36 ANSWER 44 OF 51 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:330476 HCAPLUS

DOCUMENT NUMBER: 125:104319

TITLE: Use of the yellow fever virus vaccine strain 17D for the study of strategies for the treatment of yellow fever virus infections

AUTHOR(S): Neyts, J.; Meerbach, A.; McKenna, P.; De Clercq, E.

CORPORATE SOURCE: Rega Institute for Medical Research, Katholieke Universiteit Leuven, Minderbroedersstraat 10, Louvain, B-3000, Belg.

SOURCE: Antiviral Research (1996), 30(2,3), 125-132

CODEN: ARSRDR; ISSN: 0166-3542

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have employed the attenuated vaccine strain 17D of yellow fever virus (YFV) to evaluate the inhibitory effect of a selected series of compds. on YFV in Vero cells. Use of the vaccine strain does not require high-level microbiol. containment facilities and should allow extensive screening. In addition, YFV may serve as a model for other flaviviruses including **hepatitis C virus (HCV)**, and thus strategies for the treatment of YFV infections may apply to flavivirus infections in general. In the present study, several compds. belonging to different classes of nucleoside analogs and polyanions were evaluated for their inhibitory effect on the replication of YFV. Compds. that are targeted at: (i) IMP dehydrogenase (ribavirin, EICAR, tiazofurin, selenazofurin and mycophenolic acid), (ii) OMP decarboxylase (pyrazofurin and 6-azauridine), (iii) CTP synthetase (carbodine and cyclopentenyl cytosine), (iv) dihydrofolate reductase (methotrexate) and the (v) sulfated polymers (dextran sulfate and PAVAS) proved inhibitory to the replication of YFV. Mycophenolic acid (EC₅₀: 0.08 µg/mL), EICAR (EC₅₀: 0.8 µg/mL) and methotrexate (EC₅₀: 0.07 µg/mL) were the most effective. The finding that EICAR and mycophenolic acid, despite their potent anti-YFV activity, had little or no effect on the replication of the bunyavirus Punta Toro or herpes simplex virus in Vero cells, indicates that their anti-YFV activity is rather specific and does not merely result from cytotoxicity. Inhibitors of S-adenosylhomocysteine hydrolase (SAH hydrolase) and thymidylate synthase were found to be devoid of anti-YFV activity.

CC 1-5 (Pharmacology)

Section cross-reference(s): 63

IT 54-25-1, 6-Azauridine 59-05-2, Methotrexate 9042-14-2, Dextran sulfate 24280-93-1, Mycophenolic acid 26299-60-5D, sulfated 30868-30-5, Pyrazofurin 36791-04-5, Ribavirin 60084-10-8, Tiazofurin 71184-20-8, Carbodine 83705-13-9, Selenazofurin 90597-22-1, Cyclopentenyl cytosine 118908-07-9, EICAR

RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL

(Biological study); USES (Uses)

(use of the yellow fever virus vaccine strain 17D for the study of strategies for the treatment of yellow fever virus infections)

IT 71184-20-8, Carbodine

RL: **BAC (Biological activity or effector, except adverse)**; BSU

(Biological study, unclassified); **THU (Therapeutic use)**; BIOL

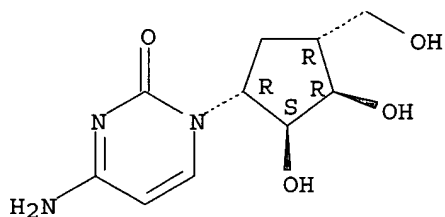
(Biological study); USES (Uses)

(use of the yellow fever virus vaccine strain 17D for the study of strategies for the treatment of yellow fever virus infections)

RN 71184-20-8 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-[(1R,2S,3R,4R)-2,3-dihydroxy-4-(hydroxymethyl)cyclopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L36 ANSWER 45 OF 51 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:200427 HCAPLUS

DOCUMENT NUMBER: 124:242295

TITLE: Compositions and methods of application of reactive antiviral polyadenylic acid derivatives

INVENTOR(S): Wang, Jui H.; Kang, Insug; Rahman, Mohammed H.

PATENT ASSIGNEE(S): USA

SOURCE: U.S., 10 pp., Cont.-in-part of U.S. Ser. No. 22,055, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5496546	A	19960305	US 1994-200650	19940223
CA 2156394	AA	19940901	CA 1994-2156394	19940223
CN 1121313	A	19960424	CN 1994-191808	19940223
CN 1078478	B	20020130		
AT 181557	E	19990715	AT 1994-909760	19940223
US 5858988	A	19990112	US 1996-604871	19960222
US 6291438	B1	20010918	US 1998-167375	19981006
PRIORITY APPLN. INFO.:			US 1993-22055	B2 19930224
			US 1994-200650	A2 19940223
			US 1996-604871	A2 19960222

AB Novel polyadenylic acid (5') derivs. with 2'-O-(3-fluoro-4,6-dinitrophenyl) groups and/or 2'-O-(2,4-dinitrophenyl) groups are synthesized and discovered to act as mutation-insensitive and function-specific inhibitors of viral reverse transcriptase. The compns., preparative procedures and methods of application of these novel compds. for the treatment of humans carrying or infected with AIDS virus and other

RNA-viruses, for the fast but temporary protection of uninfected humans and other mammals against immunodeficiency viruses and other RNA-virus caused diseases, for the preparation of a formulation containing irreversibly sterilized HIV or other RNA-viruses useful as anti-AIDS and anti-other RNA-virus disease vaccines, for the complete sterilization of possible trace amts. of live HIV and other RNA-viruses in stored transfusion blood, and for the inactivation or removal of trace amts. of RNase in solution and containers used in biotechnol. processes, are disclosed.

IC ICM A61K031-765

ICS A61K031-785

INCL 424078360

CC 63-3 (Pharmaceuticals)

IT **Hepatitis**

(A, polyadenylate derivs. for inhibition of RNA viruses and treatment of associated diseases)

IT **Hepatitis**

(C, polyadenylate derivs. for inhibition of RNA viruses and treatment of associated diseases)

IT **Virus, animal**

(**hepatitis A**, polyadenylate derivs. for inhibition of RNA viruses and treatment of associated diseases)

IT **Virus, animal**

(**hepatitis C**, polyadenylate derivs. for inhibition of RNA viruses and treatment of associated diseases)

IT 27156-07-6D, dinitrophenyl derivs.

RL: **BAC (Biological activity or effector, except adverse)**; BSU

(Biological study, unclassified); **THU (Therapeutic use)**; BIOL

(Biological study); USES (Uses)

(polyadenylate derivs. for inhibition of RNA viruses and treatment of associated diseases)

IT 27156-07-6D, dinitrophenyl derivs.

RL: **BAC (Biological activity or effector, except adverse)**; BSU

(Biological study, unclassified); **THU (Therapeutic use)**; BIOL

(Biological study); USES (Uses)

(polyadenylate derivs. for inhibition of RNA viruses and treatment of associated diseases)

RN 27156-07-6 HCAPLUS

CN 5'-Adenylic acid, homopolymer, complex with 5'-thymidylic acid homopolymer (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 25086-81-1

CMF (C10 H15 N2 O8 P)x

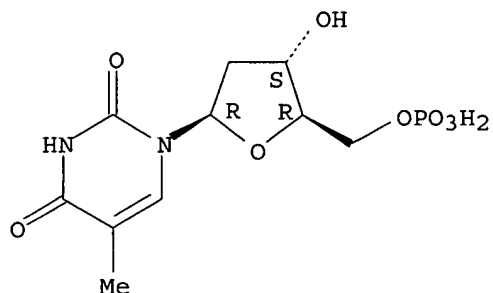
CCI PMS

CM 2

CRN 365-07-1

CMF C10 H15 N2 O8 P

Absolute stereochemistry.



CM 3

CRN 24937-83-5

CMF (C10 H14 N5 O7 P)x

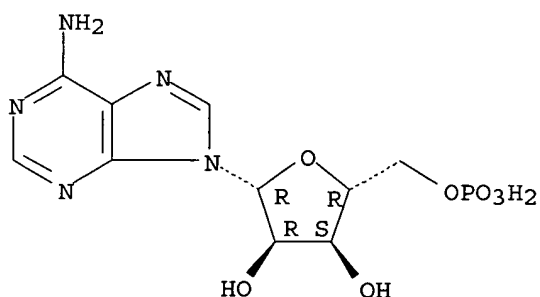
CCI PMS

CM 4

CRN 61-19-8

CMF C10 H14 N5 O7 P

Absolute stereochemistry.



L36 ANSWER 46 OF 51 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:181855 HCAPLUS

DOCUMENT NUMBER: 124:250904

TITLE: Compositions of N-(phosphonoacetyl)-L-aspartic acid (PALA) and methods of their use as broad spectrum antivirals

INVENTOR(S): Blough, Herbert A.

PATENT ASSIGNEE(S): U.S. Bioscience, Inc., USA

SOURCE: U.S., 39 pp., Cont.-in-part of U.S. Ser. No. 853,454, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

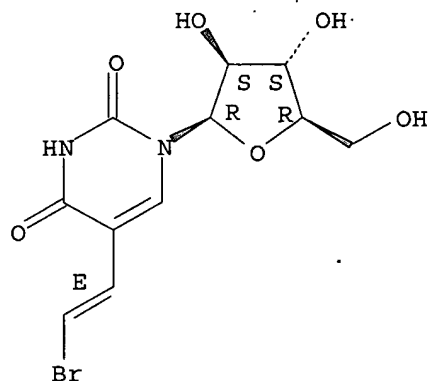
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 5491135	A	19960213	US 1993-32234	19930317
ZA 9301934	A	19930318	ZA 1993-1934	19930107
IL 105090	A1	19980816	IL 1993-105090	19930317
CA 2109435	AA	19930919	CA 1993-2109435	19930318
CA 2109435	C	19970311		
WO 9318763	A1	19930930	WO 1993-US2432	19930318
W: AU, BB, BG, BR, CA, CZ, FI, HU, JP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9339659	A1	19931021	AU 1993-39659	19930318
CN 1080853	A	19940119	CN 1993-104593	19930318
EP 660710	A1	19950705	EP 1993-909132	19930318
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07507770	T2	19950831	JP 1993-516700	19930318
BR 9306123	A	19970826	BR 1993-6123	19930318
PRIORITY APPLN. INFO.:			US 1992-853454	B2 19920318
			US 1993-32234	A 19930317
			WO 1993-US2432	A 19930318
AB Compns. and methods are disclosed which utilize the broad spectrum antiviral activity of PALA. This compound and its pharmaceutically acceptable analogs possess potent activity while displaying minimal toxicity and, therefore, are characterized by a relatively high therapeutic index. Compns. optionally containing other therapeutic agents, such as other antiviral agents, are also disclosed and are found to possess synergistic and/or additive antiviral activity.				
IC ICM A61K031-505				
INCL 514115000				
CC 1-5 (Pharmacology)				
Section cross-reference(s): 63				
IT Virus, animal				
(hepatitis B, phosphonoacetyl aspartic acid, alone or in combination with other agents, for broad spectrum antiviral, and pharmaceutical compns.)				
IT Virus, animal				
(hepatitis C, phosphonoacetyl aspartic acid, alone or in combination with other agents, for broad spectrum antiviral, and pharmaceutical compns.)				
IT 13292-46-1, Rifampicin 36791-04-5, Ribavirin 59277-89-3, Acyclovir 77181-69-2, BV-AraU 82410-32-0, Ganciclovir				
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)				
(phosphonoacetyl aspartic acid, alone or in combination with other agents, for broad spectrum antiviral, and pharmaceutical compns.)				
IT 77181-69-2, BV-AraU				
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)				
(phosphonoacetyl aspartic acid, alone or in combination with other agents, for broad spectrum antiviral, and pharmaceutical compns.)				
RN 77181-69-2 HCAPLUS				
CN 2,4(1H,3H)-Pyrimidinedione, 1-β-D-arabinofuranosyl-5-[(1E)-2-bromoethenyl]- (9CI) (CA INDEX NAME)				

Absolute stereochemistry.
Double bond geometry as shown.



L36 ANSWER 47 OF 51 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:151372 HCAPLUS

DOCUMENT NUMBER: 124:221849

TITLE: Comparative analysis of different PCR techniques for detection of *HCV* in hepatocellular carcinoma patients

AUTHOR(S): Zekri, A-R. N.; Bahnassy, A. A.; Khaled, H. M.; Mansour, O.; Attia, M. A.

CORPORATE SOURCE: Cancer Biology Department, Cairo University, Egypt

SOURCE: Cancer Journal (1995), 8(6), 331-5

CODEN: CANJEI; ISSN: 0765-7846

PUBLISHER: Association pour le Developpement de la Communication Cancerologique

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Background - The detection of *HCV*-RNA genome is at present the only direct marker for diagnosis of *HCV* infection in serum, liver, peripheral blood mononuclear cells, saliva, urine and spleen, through the use of PCR techniques. However, many factors can affect the final interpretation of the PCR results including heterogeneity of the *HCV* genome, the procedure used for isolation of the viral genome, the performance of amplification steps as well as sample contamination. Methods - In this study three different isolation procedures and a primer set from the 5'-UTR were compared using three variable PCR techniques (direct PCR, single-tube RT-PCR and semi-nested PCR). This was applied for detection of *HCV*-RNA in sera from 30 hepatocellular carcinoma patients pos. for *HCV* antibodies by both EIA (ORTHO *HCV* 2.0 ELISA) and immunoblotting (RIBA-2) technique. Results - It was found that RNA extraction with silica and semi-nested PCR technique were the most sensitive procedures. *HCV* genome was detected in 70%, 86.6%, and 86.6% of the samples using the 3 different PCR techniques after silica extraction, while the denaturation method gave the lowest yield (50%, 53.3%, and 60% resp.). The Guth method showed moderate sensitivity. By this combined method we were able to detect 20 copies of the in-vitro transcribed RNA compared to 50 copies and 100 copies using one tube RT-PCR and direct PCR techniques resp. Conclusions - The detection of *HCV*-RNA in the clin. samples is critically dependent on the quality of the RNA and efficiency of the c-DNA synthesis. The combination of one tube-extraction (silica method) and one-tube RT-PCR or even semi-nested RT-PCR minimizes the risk of false pos. results through contamination. This, together with minimal time required to individual assay as well as the ability for detect 20-50 copies of *HCV*-RNA in the clin.

specimens make our combination ideal for monitoring patients undergoing antiviral therapy and for proper diagnosis of **HCV** infection.

CC 3-1 (Biochemical Genetics)

Section cross-reference(s): 10, 14

ST **hepatitis C virus** PCR diagnosis carcinoma;

hepatocellular carcinoma diagnosis PCR **HCV** virus

IT Ribonucleic acids, viral

RL: ANT (Analyte); PUR (Purification or recovery); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(one-tube silica extraction method; comparative anal. of different PCR techniques for detection of **hepatitis C virus** in hepatocellular carcinoma patients)

IT Blood analysis

(serum; comparative anal. of different PCR techniques for detection of **hepatitis C virus** in hepatocellular carcinoma patients)

IT Polymerase chain reaction

(single-tube RT-PCR and semi-nested PCR; comparative anal. of different PCR techniques for detection of **hepatitis C virus** in hepatocellular carcinoma patients)

IT **Virus, animal**

(**hepatitis C**, comparative anal. of different PCR techniques for detection of **hepatitis C virus** in hepatocellular carcinoma patients)

IT Liver, neoplasm

(hepatoma, diagnosis; comparative anal. of different PCR techniques for detection of **hepatitis C virus** in hepatocellular carcinoma patients)

IT 174573-75-2

RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(PCR primer **HCV-6**; comparative anal. of different PCR techniques for detection of **hepatitis C virus** in hepatocellular carcinoma patients)

IT 174599-23-6

RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(PCR primer RB6A; comparative anal. of different PCR techniques for detection of **hepatitis C virus** in hepatocellular carcinoma patients)

IT 174599-24-7

RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(PCR primer RB6B; comparative anal. of different PCR techniques for detection of **hepatitis C virus** in hepatocellular carcinoma patients)

IT 174599-25-8

RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(probe RBGP; comparative anal. of different PCR techniques for detection of **hepatitis C virus** in hepatocellular carcinoma patients)

IT 174573-75-2

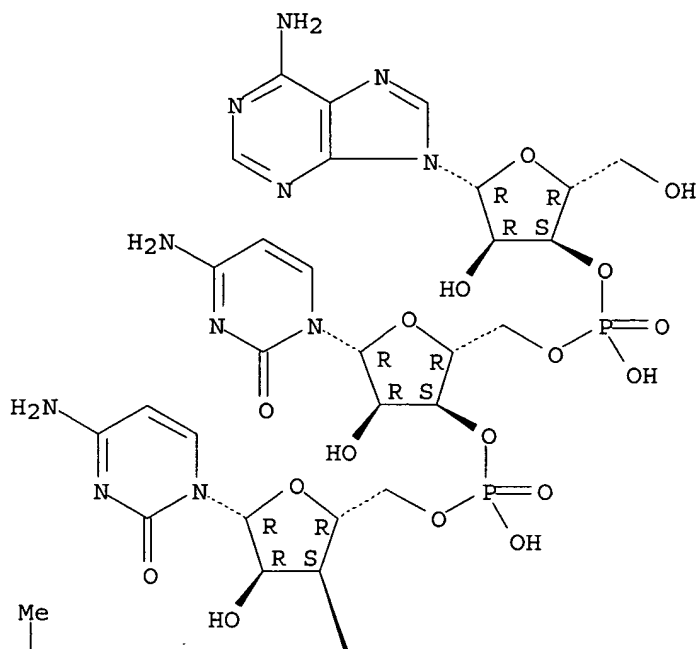
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(PCR primer **HCV-6**; comparative anal. of different PCR techniques for detection of **hepatitis C virus** in hepatocellular carcinoma patients)

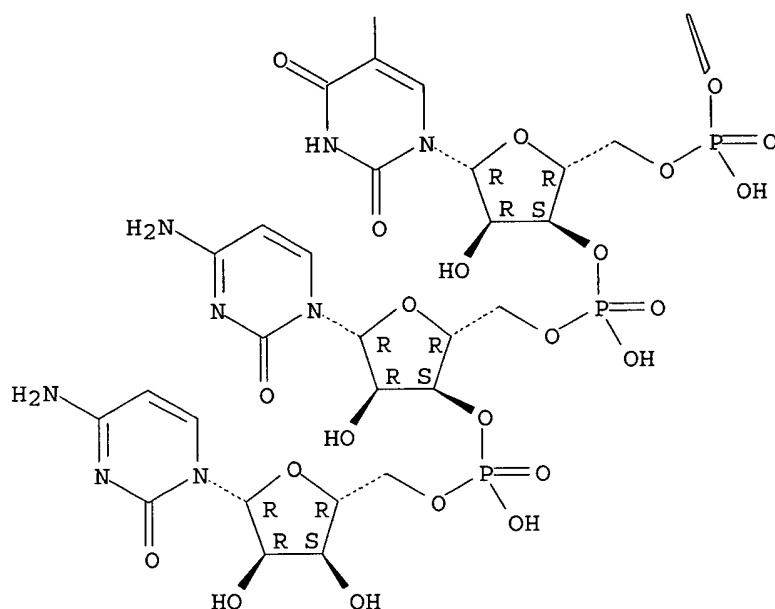
RN 174573-75-2 HCAPLUS

CN Cytidine, adenylyl-(3'→5')-cytidylyl-(3'→5')-cytidylyl-
(3'→5')-5-methyluridylyl-(3'→5')-cytidylyl-(3'→5')-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





L36 ANSWER 48 OF 51 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:748587 HCAPLUS

DOCUMENT NUMBER: 123:160183

TITLE: Efficacy of combination therapy with interferon and azidothymidine in chronic type C **hepatitis**: a pilot study

AUTHOR(S): Tsutsumi, Mikihiro; Takada, Akira; Sawada, Makoto
CORPORATE SOURCE: Dep. Int. Med., Kanazawa Med. Univ., Ishikawa, 920-02, Japan

SOURCE: Journal of Gastroenterology (1995), 30(4), 485-92
CODEN: JOGAET; ISSN: 0944-1174

PUBLISHER: Springer

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effects of interferon are seen in only a limited number of patients with **hepatitis C virus (HCV)** of the K1 type, indicating that a combination therapy with other antiviral drugs may be essential to obtain better results. In the present pilot study, the effects of combination therapy with interferon (IFN) and an antiviral drug azidothymidine (AZT) were analyzed. The combination therapy was conducted in 22 patients with chronic **hepatitis C** after obtaining their informed consent (combination group). Three of six million units of natural IFN alpha was administered daily for 3 wk and then three times a week for 21 wk. Combination therapy was initiated at the beginning of the 8th week of IFN treatment, 500 mg of AZT per day being given for 8 wk. As a control, changes in **HCV**-RNA were also analyzed in patients treated with interferon alone (IFN-alone group). At the end of the treatment, blood was neg. for **HCV** in 32.5% of the IFN-alone group and in 50.0% of the combination group, the difference not being significant. However, in patients with **HCV**-K1, **HCV**-neg. rates were 14.2% in the IFN-alone group and 45.5% in the combination group, showing a significant difference. In patients with other **HCV** genotypes, **HCV**-neg. rates did not differ between

the two groups. These results suggest that combination therapy with IFN and AZT may be an effective treatment for chronic type C **hepatitis** caused by the K1 type virus, although further studies on larger number of patients will be needed to obtain definite conclusions.

CC 1-5 (Pharmacology)

ST interferon azidothymidine virucide chronic **hepatitis** C

IT Virucides and Virustats

(combination therapy efficacy of interferon and azidothymidine in chronic type C **hepatitis** in humans)

IT Interferons

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(combination therapy efficacy of interferon and azidothymidine in chronic type C **hepatitis** in humans)

IT **Hepatitis**

(C, chronic, combination therapy efficacy of interferon and azidothymidine in chronic type C **hepatitis** in humans)

IT 30516-87-1, Azidothymidine

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(combination therapy efficacy of interferon and azidothymidine in chronic type C **hepatitis** in humans)

IT 30516-87-1, Azidothymidine

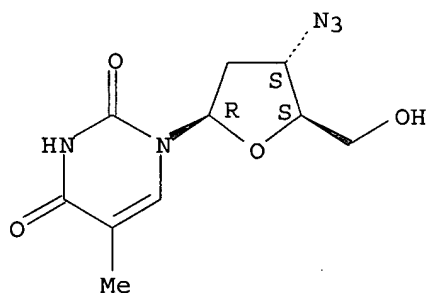
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(combination therapy efficacy of interferon and azidothymidine in chronic type C **hepatitis** in humans)

RN 30516-87-1 HCAPLUS

CN Thymidine, 3'-azido-3'-deoxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L36 ANSWER 49 OF 51 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:621975 HCAPLUS

DOCUMENT NUMBER: 121:221975

TITLE: Compositions, preparation, and methods of application of reactive (fluoro)dinitrophenyl polyadenylic acid derivatives for inhibition of RNA viruses

INVENTOR(S): Wang, Jui H.; Kang, Insung; Raham, Mohammed H.

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 38 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 4
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9419012	A2	19940901	WO 1994-US1913	19940223
WO 9419012	A3	19941027		
W: AU, CA, CN, JP, KR				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2156394	AA	19940901	CA 1994-2156394	19940223
AU 9462475	A1	19940914	AU 1994-62475	19940223
EP 686043	A1	19951213	EP 1994-909760	19940223
EP 686043	B1	19990623		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1121313	A	19960424	CN 1994-191808	19940223
CN 1078478	B	20020130		
AT 181557	E	19990715	AT 1994-909760	19940223
PRIORITY APPLN. INFO.:			US 1993-22055	A 19930224
			WO 1994-US1913	W 19940223

AB Novel polyadenylic acid (5') derivs. with 2'-O-(3-fluoro-4,6-dinitrophenyl) groups and/or 2'-O-(2,4-dinitrophenyl) groups have been synthesized and discovered to act as mutation-insensitive and function-specific inhibitors of viral reverse transcriptase. The compns., preparative procedures, and methods of application of these novel compds. for the treatment of humans carrying or infected with AIDS virus and other RNA-viruses and of other mammals carrying RNA-viruses, for the fast but temporary protection of uninfected humans and other mammals against immunodeficiency viruses and other RNA-virus-caused diseases, for the preparation of a formulation containing irreversibly sterilized HIV or other RNA-viruses useful as anti-AIDS and anti-other RNA-virus disease vaccines, for the complete sterilization of possible trace amts. of live HIV and other RNA-viruses in stored transfusion blood, and for the inactivation or removal of trace amts. of RNase in solution and containers used in biotechnol. processes have all been disclosed.

IC ICM A61K039-12

ICS A61K039-29; A61K039-44

CC 1-5 (Pharmacology)

Section cross-reference(s): 15, 33

IT **Hepatitis**

(A, compns., preparation, and methods of application of reactive (fluoro)dinitrophenyl polyadenylic acid derivs. for inhibition of RNA viruses and treatment of associated diseases)

IT **Hepatitis**

(C, compns., preparation, and methods of application of reactive (fluoro)dinitrophenyl polyadenylic acid derivs. for inhibition of RNA viruses and treatment of associated diseases)

IT Virus, animal

(**hepatitis A**, compns., preparation, and methods of application of reactive (fluoro)dinitrophenyl polyadenylic acid derivs. for inhibition of RNA viruses)

IT **Virus, animal**

(**hepatitis C**, compns., preparation, and methods of application of reactive (fluoro)dinitrophenyl polyadenylic acid derivs. for inhibition of RNA viruses)

IT 27156-07-6D, Poly(A)-poly(dT), dinitrophenyl derivs.

RL: **BAC (Biological activity or effector, except adverse)**; BSU

(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); USES (Uses)
(dinitrophenyl polyadenylic acid derivative inhibition of HIV-1 virus
reverse transcriptase)

IT 27156-07-6D, Poly(A)-poly(dT), dinitrophenyl derivs.

RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); USES (Uses)

(dinitrophenyl polyadenylic acid derivative inhibition of HIV-1 virus
reverse transcriptase)

RN 27156-07-6 HCAPLUS

CN 5'-Adenylic acid, homopolymer, complex with 5'-thymidylic acid homopolymer
(1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 25086-81-1

CMF (C10 H15 N2 O8 P)x

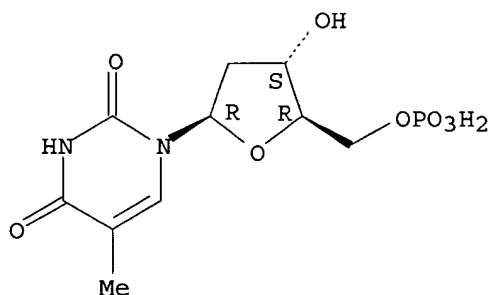
CCI PMS

CM 2

CRN 365-07-1

CMF C10 H15 N2 O8 P

Absolute stereochemistry.



CM 3

CRN 24937-83-5

CMF (C10 H14 N5 O7 P)x

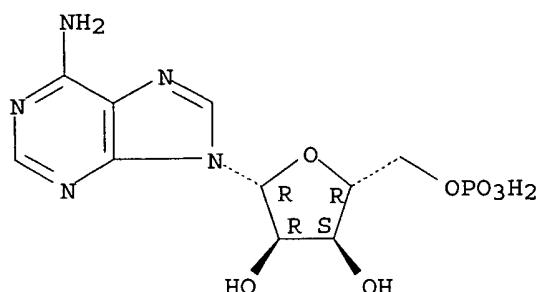
CCI PMS

CM 4

CRN 61-19-8

CMF C10 H14 N5 O7 P

Absolute stereochemistry.



L36 ANSWER 50 OF 51 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:648179 HCAPLUS
DOCUMENT NUMBER: 117:248179
TITLE: Nucleoside-polypeptide conjugates with 3' ester linkage for treatment of tumors and viral diseases
INVENTOR(S): Pietersz, Geoffrey
PATENT ASSIGNEE(S): Austin Research Institute, Australia
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9214758	A1	19920903	WO 1992-AU47	19920213
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
AU 9212453	A1	19920915	AU 1992-12453	19920213
PRIORITY APPLN. INFO.:			AU 1991-4585	A 19910213
			WO 1992-AU47	A 19920213

OTHER SOURCE(S): MARPAT 117:248179

AB Nucleoside conjugates with polypeptides (antibodies, hormones, growth factors, biol. active peptides) are provided in which the nucleoside is coupled to the polypeptide via a 3' ester linkage. The conjugates may be used in the treatment of tumors or viral diseases. 2'-Deoxy-5-fluoro-3'-O-succinoyluridine (preparation given) was converted to an active ester derivative

and then coupled with a monoclonal antibody against murine Ly-2.1 antigen. The cytotoxicity of the conjugates with 2-20 mols. of 2'-deoxy-5-fluorouridine bound per antibody mol. were tested on LY-2.1+ E3 and LY-2.1- BW cell lines; IC50 values were 5.0 ± 10^{-9} - 9.0×10^{-9} M and 2 ± 10^{-8} - 6×10^{-8} M, resp. In vivo activity of the conjugate is also reported.

IC ICM C07K015-12
ICS C07K015-18; C07K015-28; C07K017-02; C07K017-06; C07H021-02; C07H021-04; A61K039-44

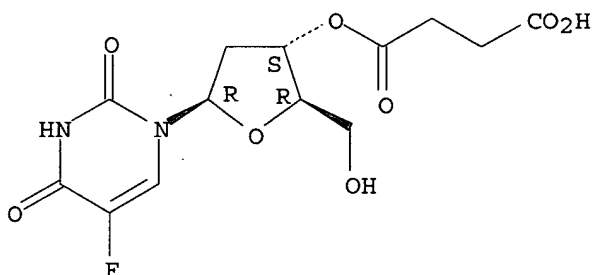
CC 9-14 (Biochemical Methods)
Section cross-reference(s): 1, 33, 63

IT Virus, animal
(hepatitis A, infection with, treatment of, nucleoside-polypeptide conjugates with 3' ester link for)

IT Virus, animal
(hepatitis B, infection with, treatment of,

nucleoside-polypeptide conjugates with 3' ester link for)
IT **Virus, animal**
(**hepatitis C**, infection with, treatment of,
nucleoside-polypeptide conjugates with 3' ester link for)
IT **Virus, animal**
(**hepatitis D**, infection with, treatment of,
nucleoside-polypeptide conjugates with 3' ester link for)
IT **Virus, animal**
(**hepatitis E**, infection with, treatment of,
nucleoside-polypeptide conjugates with 3' ester link for)
IT **133349-29-8DP**, monoclonal antibody conjugates
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); SPN (Synthetic preparation); BIOL
(Biological study); PREP (Preparation)
(preparation of and cytotoxic and antitumor activity of)
IT **133349-29-8DP**, monoclonal antibody conjugates
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); SPN (Synthetic preparation); BIOL
(Biological study); PREP (Preparation)
(preparation of and cytotoxic and antitumor activity of)
RN 133349-29-8 HCAPLUS
CN Uridine, 2'-deoxy-5-fluoro-, 3'-(hydrogen butanedioate) (9CI) (CA INDEX
NAME)

Absolute stereochemistry.



L36 ANSWER 51 OF 51 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:609146 HCAPLUS
DOCUMENT NUMBER: 111:209146
TITLE: Use of 1-(2-deoxy-2-fluoro- β -D-arabinofuranosyl)-
5-ethyluracil as virucide for the inhibition of
hepatitis virus
INVENTOR(S): Fox, Jack J.; Watanabe, Kyoichi A.; Lopez, Carlos;
Trepo, Christian G.
PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA;
Institut National de la Sante et de la Recherche
Medicale (INSERM)
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 8901776	A1	19890309	WO 1988-US3035	19880902
W: AU, JP, KR, NO				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
IL 87646	A1	19940731	IL 1988-87646	19880901
AU 8824876	A1	19890331	AU 1988-24876	19880902
EP 338042	A1	19891025	EP 1988-908588	19880902
EP 338042	B1	19931020		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 02500524	T2	19900222	JP 1988-507929	19880902
ES 2014042	A6	19900616	ES 1988-2716	19880902
AT 96029	E	19931115	AT 1988-908588	19880902
KR 9711386	B1	19970710	KR 1989-70795	19890503
PRIORITY APPLN. INFO.:			US 1987-92446	A 19870903
			EP 1988-908588	A 19880902
			WO 1988-US3035	A 19880902

AB Pharmaceuticals for the treatment of **hepatitis** virus infections comprise the title compound (I) or its salts and carriers. Also, a prodrug form of I may be used as the active agent. The **hepatitis** virus may be **hepatitis A**, **hepatitis B** or non-A, non-B **hepatitis** virus. I was used in the woodchuck **hepatitis** model for testing potential antihepatitis B activity in humans and inhibited the woodchuck **hepatitis** virus via the oral route. The 5-methyl analog also inhibited woodchuck **hepatitis** virus, but also exhibited unacceptable toxicity at the same dose as I. Pharmaceuticals preferably contain 0.04-50 mg/kg I (no data). I was effective in the treatment of simian varicella virus in african green monkeys via the oral and i.v. route.

IC ICM A61K031-70
ICS C07H019-06; C07H019-10

CC 1-5 (Pharmacology)

ST deoxyfluoroarabinofuranosylethyluracil virucide; uracil
deoxyfluoroarabinofuranosylethyl **hepatitis**; **hepatitis**
deoxyfluoroarabinofuranosylethyluracil

IT Virus, animal
(**hepatitis A**, infection with, treatment of,
(deoxyfluoroarabinofuranosyl)ethyluracil for)

IT Virus, animal
(**hepatitis B**, infection with, treatment of,
(deoxyfluoroarabinofuranosyl)ethyluracil for)

IT Virus, animal
(**hepatitis, non-A, non-B**, infection with, treatment of, (deoxyfluoroarabinofuranosyl)ethyluracil for)

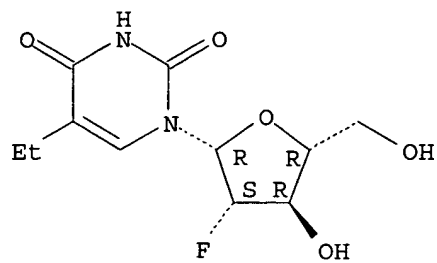
IT 83546-42-3
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); BIOL (Biological study)
(virucide, for **hepatitis** treatment)

IT 83546-42-3
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); BIOL (Biological study)
(virucide, for **hepatitis** treatment)

RN 83546-42-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro- β -D-arabinofuranosyl)-
5-ethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d his nofile

(FILE 'HOME' ENTERED AT 10:01:20 ON 25 AUG 2006)

FILE 'CAPLUS' ENTERED AT 10:01:41 ON 25 AUG 2006

E US2003-632875/APPS

L1 2 SEA ABB=ON PLU=ON US2003-632875/AP
D SCAN

FILE 'REGISTRY' ENTERED AT 10:06:09 ON 25 AUG 2006

L2 STRUCTURE UPLOADED

D QUE L2

L3 50 SEA SSS SAM L2

L4 109180 SEA SSS FUL L2

SAVE L4 KHARE875/A TEMP

FILE 'CAPLUS' ENTERED AT 10:07:52 ON 25 AUG 2006

L5 94725 SEA ABB=ON PLU=ON L4
SEL RN L1

FILE 'REGISTRY' ENTERED AT 10:08:33 ON 25 AUG 2006

L6 166 SEA ABB=ON PLU=ON (119567-79-2/BI OR 121154-51-6/BI OR
147058-39-7/BI OR 198153-51-4/BI OR 206269-27-4/BI OR 220581-49
-7/BI OR 223603-41-6/BI OR 254750-02-2/BI OR 36791-04-5/BI OR
402957-28-2/BI OR 472960-22-8/BI OR 56-92-8/BI OR 62304-98-7/BI
OR 768-94-5/BI OR 10380-93-5/BI OR 107-20-0/BI OR 107036-57-7/
BI OR 108-24-7/BI OR 118390-30-0/BI OR 128075-94-5/BI OR
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8/BI OR 150938-57-1/BI OR 153547-97-8/BI OR 153547-98-9/BI OR
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4137-57-9/BI OR 415704-30-2/BI OR 51172-83-9/BI OR 52813-63-5/B
I OR 53558-93-3/BI OR 5418-51-9/BI OR 54503-61-6/BI OR
57071-82-6/BI OR 57901-59-4/BI OR 57901-63-0/BI OR 57901-65-2/B
I OR 57901-66-3/BI OR 57901-71-0/BI OR 58-96-8/BI OR 58479-61-1
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-9/BI OR 656808-99-0/BI OR 656809-00-6/BI OR 656809-02-8/BI OR
656809-04-0/BI OR 656809

L7 31 SEA ABB=ON PLU=ON L6 AND L4
D SCAN

FILE 'CAPLUS' ENTERED AT 10:10:29 ON 25 AUG 2006

L8 6985 SEA ABB=ON PLU=ON L7

FILE 'CAPLUS' ENTERED AT 10:13:55 ON 25 AUG 2006

D SCAN L1

FILE 'REGISTRY' ENTERED AT 10:14:57 ON 25 AUG 2006

FILE 'CAPLUS' ENTERED AT 10:15:00 ON 25 AUG 2006

L9 17230 SEA ABB=ON PLU=ON L4 (L) (PAC OR THU OR BAC OR PKT OR
DMA)/RL

FILE 'HCAPLUS' ENTERED AT 10:16:01 ON 25 AUG 2006

E HCV/CT

E E3+ALL

L10 12372 SEA ABB=ON PLU=ON (HCV+PFT/CT OR "CLASSICAL SWINE FEVER
VIRUS"+PFT/CT OR "HEPATITIS C VIRUS"+PFT/CT)
E HEPATITIS C/CT

E E5+ALL

L11 11667 SEA ABB=ON PLU=ON "HEPATITIS C VIRUS"+PFT/CT

L12 15162 SEA ABB=ON PLU=ON (HCV OR H(1A)C(1A)V OR HEPATITIS C
VIRUS?)/OBI,BI

L13 90130 SEA ABB=ON PLU=ON ((VIRAL?)/OBI,BI

L14 55395 SEA ABB=ON PLU=ON (ANTIVIRAL?)/OBI,BI

L15 4441 SEA ABB=ON PLU=ON L9 AND (L10 OR L11 OR L12 OR L13 OR L14)

L16 247 SEA ABB=ON PLU=ON L9 AND (L10 OR L11 OR L12)

L17 53 SEA ABB=ON PLU=ON L16 NOT (PY>2002 OR AY>2002 OR PRY>2002)

FILE 'REGISTRY' ENTERED AT 10:20:51 ON 25 AUG 2006

L18 STRUCTURE UPLOADED

L19 50 SEA SUB=L4 SSS SAM L18

FILE 'STNGUIDE' ENTERED AT 10:21:24 ON 25 AUG 2006

FILE 'REGISTRY' ENTERED AT 10:24:46 ON 25 AUG 2006

L20 STRUCTURE UPLOADED

L21 32 SEA SUB=L4 SSS SAM L20

L22 779 SEA SUB=L4 SSS FUL L20
SAVE L22 DEVESH875/A TEMP

FILE 'CAPLUS' ENTERED AT 10:25:44 ON 25 AUG 2006

L23 279 SEA ABB=ON PLU=ON L22 (L) (PAC OR THU OR BAC OR PKT OR
DMA)/RL

FILE 'HCAPLUS' ENTERED AT 10:26:29 ON 25 AUG 2006

L24 20 SEA ABB=ON PLU=ON L23 AND (L10 OR L11 OR L12)

L25 1 SEA ABB=ON PLU=ON L24 NOT (PY>2002 OR AY>2002 OR PRY>2002)

FILE 'STNGUIDE' ENTERED AT 10:27:09 ON 25 AUG 2006

FILE 'HCAPLUS' ENTERED AT 10:31:23 ON 25 AUG 2006

L26 177 SEA ABB=ON PLU=ON L23 NOT (PY>2002 OR AY>2002 OR PRY>2002)

L27 168 SEA ABB=ON PLU=ON L23 AND (L10 OR L11 OR L12 OR L13 OR L14)

L28 20 SEA ABB=ON PLU=ON L27 AND (L10 OR L11 OR L12)

L29 1 SEA ABB=ON PLU=ON L28 NOT (PY>2002 OR AY>2002 OR PRY>2002)

FILE 'REGISTRY' ENTERED AT 10:37:08 ON 25 AUG 2006

FILE 'HCAPLUS' ENTERED AT 10:37:58 ON 25 AUG 2006

D BIB L28 1

D BIB L26 1

L30 59 SEA ABB=ON PLU=ON L27 AND (HEPATITIS? OR HCV? OR H(1A)C(1A)V?
)

D BIB L30 1

D BIB L30 2
L31 170 SEA ABB=ON PLU=ON L23 NOT (PY>2001 OR AY>2001 OR PRY>2001)
D BIB 1
L32 177 SEA ABB=ON PLU=ON (L26 OR L31)
L33 20 SEA ABB=ON PLU=ON L30 AND L24
L34 59 SEA ABB=ON PLU=ON (L30 OR L33)
L35 52 SEA ABB=ON PLU=ON L17 NOT L34
L36 51 SEA ABB=ON PLU=ON L35 AND (HEPATITIS? OR HCV? OR H(1A)C(1A)V?
)
E SCHINAZI R/AU
L37 511 SEA ABB=ON PLU=ON ("SCHINAZI R"/AU OR "SCHINAZI R F"/AU OR
"SCHINAZI RAYMOND"/AU OR "SCHINAZI RAYMOND F"/AU OR "SCHINAZI
RAYMOND FELIX"/AU OR "SCHINAZI REYMOND F"/AU)
E STRIKER R/AU
L38 14 SEA ABB=ON PLU=ON ("STRIKER R"/AU OR "STRIKER ROBERT"/AU OR
"STRIKER ROBERT T"/AU)
E SHI J/AU
L39 6019 SEA ABB=ON PLU=ON SHI J?/AU
L40 30 SEA ABB=ON PLU=ON (L37 AND (L38 OR L39)) OR (L38 AND L39)

FILE 'REGISTRY' ENTERED AT 10:50:50 ON 25 AUG 2006

FILE 'HCAPLUS' ENTERED AT 10:50:53 ON 25 AUG 2006

D QUE L40
D IBIB ABS L40 TOT
D QUE L34
D IBIB ABS HITIND HITSTR L34 TOT
D QUE L36
D IBIB ABS HITIND HITSTR L36 31-51

FILE 'REGISTRY' ENTERED AT 11:19:19 ON 25 AUG 2006

L41 STRUCTURE UPLOADED
L42 12 SEA SUB=L4 SSS SAM L41
L43 347 SEA SUB=L4 SSS FUL L41

FILE 'HCAPLUS' ENTERED AT 11:19:59 ON 25 AUG 2006

L44 1048 SEA ABB=ON PLU=ON L43
L45 259 SEA ABB=ON PLU=ON L44 (L) (PAC OR THU OR BAC OR PKT OR
DMA)/RL
L46 259 SEA ABB=ON PLU=ON L43 (L) (PAC OR THU OR BAC OR PKT OR
DMA)/RL
L47 157 SEA ABB=ON PLU=ON L46 AND (L10 OR L11 OR L12 OR L13 OR L14)
L48 98 SEA ABB=ON PLU=ON L47 NOT (PY>2002 OR AY>2002 OR PRY>2002)
L49 23 SEA ABB=ON PLU=ON L48 AND (HEPATITIS? OR HCV? OR H(1A)C(1A)V?
)
L50 0 SEA ABB=ON PLU=ON L49 NOT (L34 OR L40)
L51 290 SEA ABB=ON PLU=ON (L46 OR L34 OR L40)
L52 203 SEA ABB=ON PLU=ON L46 NOT (L34 OR L40)
L53 157 SEA ABB=ON PLU=ON L47 AND (L10 OR L11 OR L12 OR L13 OR L14)
L54 101 SEA ABB=ON PLU=ON L52 AND (L10 OR L11 OR L12 OR L13 OR L14)
L55 75 SEA ABB=ON PLU=ON L54 NOT (PY>2002 OR AY>2002 OR PRY>2002)
L56 75 SEA ABB=ON PLU=ON L55 NOT (L34 OR L40)
L57 75 SEA ABB=ON PLU=ON L56 NOT L36
L58 0 SEA ABB=ON PLU=ON L57 AND (HEPATITIS C OR HCV? OR H(1A)C(1A)V
?)

FILE 'STNGUIDE' ENTERED AT 11:24:27 ON 25 AUG 2006

FILE 'REGISTRY' ENTERED AT 11:25:50 ON 25 AUG 2006

L59 STRUCTURE UPLOADED
L60 1 SEA SUB=L4 SSS SAM L59
L61 15 SEA SUB=L4 SSS FUL L59

FILE 'HCAPLUS' ENTERED AT 11:26:27 ON 25 AUG 2006
L62 96 SEA ABB=ON PLU=ON L61
L63 54 SEA ABB=ON PLU=ON L61 (L) (PAC OR THU OR BAC OR PKT OR
DMA)/RL
L64 44 SEA ABB=ON PLU=ON L63 AND (L10 OR L11 OR L12 OR L13 OR L14)
L65 29 SEA ABB=ON PLU=ON L63 NOT (L34 OR L40)
L66 19 SEA ABB=ON PLU=ON L64 NOT (L34 OR L40)
L67 29 SEA ABB=ON PLU=ON (L65 OR L66)
L68 20 SEA ABB=ON PLU=ON L67 NOT (PY>2002 OR AY>2002 OR PRY>2002)
L69 29 SEA ABB=ON PLU=ON L67 NOT L36

=> file hcaplus

FILE 'HCAPLUS' ENTERED AT 11:28:14 ON 25 AUG 2006
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 25 Aug 2006 VOL 145 ISS 10
FILE LAST UPDATED: 24 Aug 2006 (20060824/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que l69

L2 STR

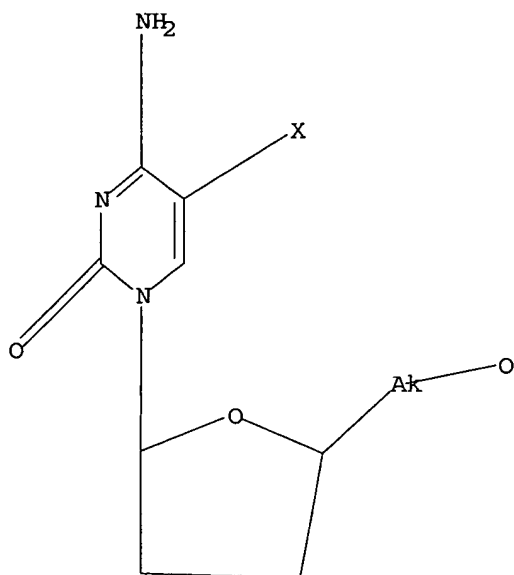
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

L4 109180 SEA FILE=REGISTRY SSS FUL L2
L9 17230 SEA FILE=CAPLUS ABB=ON PLU=ON L4 (L) (PAC OR THU OR BAC OR
PKT OR DMA)/RL
L10 12372 SEA FILE=HCAPLUS ABB=ON PLU=ON (HCV+PFT/CT OR "CLASSICAL
SWINE FEVER VIRUS"+PFT/CT OR "HEPATITIS C VIRUS"+PFT/CT)
L11 11667 SEA FILE=HCAPLUS ABB=ON PLU=ON "HEPATITIS C VIRUS"+PFT/CT
L12 15162 SEA FILE=HCAPLUS ABB=ON PLU=ON (HCV OR H(1A)C(1A)V OR
HEPATITIS C VIRUS?)/OBI,BI
L13 90130 SEA FILE=HCAPLUS ABB=ON PLU=ON ((VIRAL?)/OBI,BI
L14 55395 SEA FILE=HCAPLUS ABB=ON PLU=ON (ANTIVIRAL?)/OBI,BI
L16 247 SEA FILE=HCAPLUS ABB=ON PLU=ON L9 AND (L10 OR L11 OR L12)
L17 53 SEA FILE=HCAPLUS ABB=ON PLU=ON L16 NOT (PY>2002 OR AY>2002
OR PRY>2002)

L20

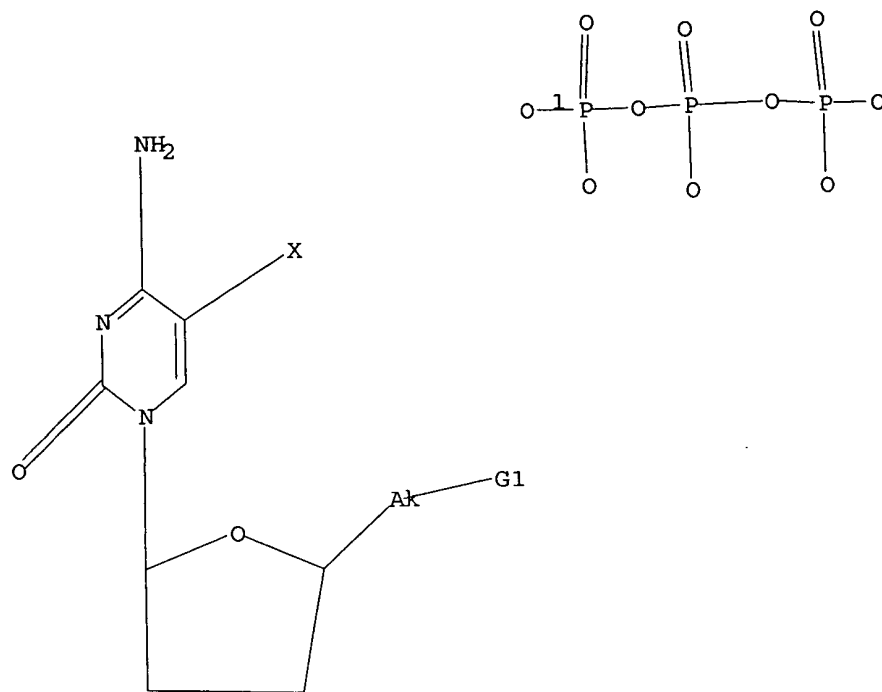
STR



Structure attributes must be viewed using STN Express query preparation.

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L23      279 SEA FILE=CAPLUS ABB=ON  PLU=ON  L22 (L) (PAC OR THU OR BAC OR
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L24      20  SEA FILE=HCAPLUS ABB=ON  PLU=ON  L23 AND (L10 OR L11 OR L12)
L27      168 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L23 AND (L10 OR L11 OR L12 OR
          L13 OR L14)
L30      59  SEA FILE=HCAPLUS ABB=ON  PLU=ON  L27 AND (HEPATITIS? OR HCV?
          OR H(1A)C(1A)V?)
L33      20  SEA FILE=HCAPLUS ABB=ON  PLU=ON  L30 AND L24
L34      59  SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L30 OR L33)
L35      52  SEA FILE=HCAPLUS ABB=ON  PLU=ON  L17 NOT L34
L36      51  SEA FILE=HCAPLUS ABB=ON  PLU=ON  L35 AND (HEPATITIS? OR HCV?
          OR H(1A)C(1A)V?)
L37      511 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("SCHINAZI R"/AU OR "SCHINAZI
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          "SCHINAZI RAYMOND FELIX"/AU OR "SCHINAZI REYMOND F"/AU)
L38      14  SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("STRIKER R"/AU OR "STRIKER
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L39      6019 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SHI J?/AU
L40      30  SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L37 AND (L38 OR L39)) OR
          (L38 AND L39)
L59      STR
  
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G1 OH, [01]

Structure attributes must be viewed using STN Express query preparation.

L61	15	SEA	FILE=REGISTRY	SUB=L4	SSS	FUL	L59
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L64	44	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L63 AND (L10 OR L11 OR L12 OR L13 OR L14)	
L65	29	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L63 NOT (L34 OR L40)	
L66	19	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L64 NOT (L34 OR L40)	
L67	29	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	(L65 OR L66)	
L69	29	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L67 NOT L36	

=> d ibib abs hitind hitstr l69 tot

L69 ANSWER 1 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:469839 HCAPLUS

DOCUMENT NUMBER: 144:488682

TITLE: Piperazine derivatives and their preparation, pharmaceutical compositions and use as CCR5 antagonists for treatment of human immunodeficiency virus or inflammatory diseases

INVENTOR(S): Ramanathan, Ragulan; Ghosal, Anima; Miller, Michael W.; Chowdhury, Swapan K.; Alton, Kevin B.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 78 pp., Cont.-in-part of U.S. Ser. No. 668,862.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006105964	A1	20060518	US 2005-255643	20051021
US 6391865	B1	20020521	US 2000-562814	20000501
US 2003069252	A1	20030410	US 2002-61011	20020130
US 6689765	B2	20040210		
US 2004067961	A1	20040408	US 2003-668862	20030923
PRIORITY APPLN. INFO.:			US 1999-132509P	P 19990504
			US 2000-562814	A3 20000501
			US 2002-61011	A3 20020130
			US 2003-668862	A2 20030923

OTHER SOURCE(S): MARPAT 144:488682

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The use of CCR5 antagonists of formula I or a pharmaceutically acceptable salt thereof, wherein R is (un)substituted Ph, pyridyl, thiophenyl or naphthyl; R1 is hydrogen or alkyl; R2 is substituted Ph, substituted heteroaryl, naphthyl, fluorenyl, diphenylmethyl or (un)substituted phenyl- or heteroaryl-alkyl; R3 is hydrogen, alkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, or (un)substituted Ph, phenylalkyl, naphthyl, naphthylalkyl, heteroaryl or heteroarylalkyl; R4, R5 and R7 are hydrogen or alkyl; R6 is hydrogen, alkyl or alkenyl; for the treatment of HIV, solid organ transplant rejection, graft v. host disease, arthritis, rheumatoid arthritis, inflammatory bowel disease, atopic dermatitis, psoriasis, asthma, allergies or multiple sclerosis is disclosed, as well as novel compds., pharmaceutical compns. comprising them, and the combination of CCR5 antagonists of the invention in combination with **antiviral** agents useful in the treatment of HIV or agents useful in the treatment of inflammatory diseases. Example compound II•HCl was prepared by methylation of Et diacetoacetate; the resulting Et 2-acetyl-3-methoxy-2-butenate underwent cyclization with formamidine to give Et 4,6-dimethyl-5-pyrimidinecarboxylate, which underwent hydrolysis to give the corresponding acid, which reacted with amine III to give compound II, which was converted to II•HCl. All the invention compds. were evaluated for their CCR5 membrane binding affinity. From the assays to determine inhibition or RANTES binding, it was found that compound II•HCl exhibited a K_i value of 2.95 nM.

INCL 514023000; 514252180; 536017400; 544295000

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 63

IT Allergy inhibitors

Anti-AIDS agents

Anti-inflammatory agents

Antiarthritics

Antiasthmatics

Antirheumatic agents

Antiviral agents

Blood plasma

Combination chemotherapy

Feces

Human

Human immunodeficiency virus

Human immunodeficiency virus 1
Monkey
Rattus
Urine

(preparation of piperazine derivs. and their use as CCR5 antagonists for treatment of human immunodeficiency virus or inflammatory diseases)

IT 127-07-1, Hydroxyurea 3056-17-5, Stavudine 7481-89-2, Zalcitabine 30516-87-1, Zidovudine 36791-04-5, Ribavirin 69655-05-6, Didanosine 110143-10-7, Lodenosine 127759-89-1, Lobucavir 127779-20-8, Saquinavir 129618-40-2, Nevirapine 134678-17-4, Lamivudine 136470-78-5, Abacavir 136817-59-9, Delavirdine 142340-99-6, Adefovir dipivoxil 142632-32-4, (+)-Calanolide A 142632-33-5, (+)-Calanolide B 143338-12-9 143491-57-0, Emtricitabine 145514-04-1, DAPD 147058-39-7 149950-60-7, MKC-442 150378-17-9, Indinavir 154598-52-4, Efavirenz 155213-67-5, Ritonavir 159519-65-0, Pentafuside 159989-64-7, Nelfinavir 161814-49-9, Amprenavir 175385-62-3, Lasinavir 177932-89-7, DMP-450 178979-85-6 185220-03-5, PNU-142721 192725-17-0, ABT-378 443862-70-2, BMS 2322623 443862-71-3, Yissum 11607

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of piperazine derivs. and their use as CCR5 antagonists for treatment of human immunodeficiency virus or inflammatory diseases)

IT 147058-39-7

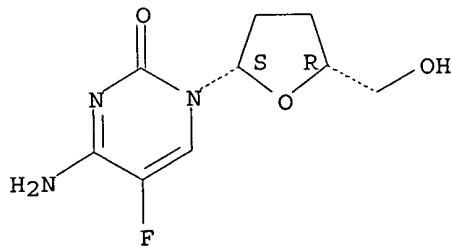
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of piperazine derivs. and their use as CCR5 antagonists for treatment of human immunodeficiency virus or inflammatory diseases)

RN 147058-39-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L69 ANSWER 2 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:962084 HCAPLUS

DOCUMENT NUMBER: 143:272372

TITLE: Compositions containing gap junction communication-enhancing aromatic acids and nucleoside analog prodrugs for enhanced cancer therapy

INVENTOR(S): Ekstroem, Tomas J.; Almqvist, Per M.; Asklund, Thomas

PATENT ASSIGNEE(S): Zgene A/S, Den.

SOURCE: PCT Int. Appl., 71 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005079849	A2	20050901	WO 2005-EP50805	20050225
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
PRIORITY APPLN. INFO.:			DK 2004-302	A 20040225
			US 2004-547058P	P 20040225

OTHER SOURCE(S): MARPAT 143:272372

AB The present invention relates to methods and compns. for enhanced cancer treatment based on nucleoside analog prodrugs. Thus, aromatic organic acids which enhance gap junction communication are combined with nucleoside analog prodrugs to improve anticancer therapy. Thus, 4-phenylbutyrate increased expression of GFAP and connexin 43 and enhanced gap junction communication in glioblastoma multiforme cells. The efficacy of AZT in these cells was increased by 4-phenylbutyrate in the presence or absence of deoxynucleoside kinase.

IC ICM A61K045-06

ICS A61K031-192; A61K031-7052; A61P035-00; A61K038-45

CC 63-3 (Pharmaceuticals)

Section cross-reference(s): 1

IT Antitumor agents

Bladder, neoplasm

Esophagus, neoplasm

Gene therapy

Human

Lung, neoplasm

Mammary gland, neoplasm

Melanoma

Ovary, neoplasm

Prostate gland, neoplasm

Tongue, neoplasm

Viral vectors

(compns. containing gap junction communication-enhancing aromatic acids and nucleoside analog prodrugs for enhanced cancer therapy)

IT 50-90-8, 5-Chloro-2'-deoxyuridine 50-91-9, 5-Fluoro-2'-deoxyuridine

54-42-2, Idoxuridine 59-14-3, 5-Bromo-2'-deoxyuridine 70-00-8,

Trifluorothymidine 73-03-0, 3'-Deoxyadenosine 86-87-3,

1-Naphthylacetic acid 90-27-7, 2-Phenylbutyric acid 90-64-2,

 α -Hydroxyphenylacetic acid 99-66-1, Valproic acid 103-82-2,

Phenylacetic acid, biological studies 107-92-6, Butanoic acid,

biological studies 122-59-8, Phenoxyacetic acid 147-94-4, Ara-C

405-50-5, 4-Fluorophenylacetic acid 492-37-5, α -Methylphenylacetic

acid 501-52-0, Benzenepropanoic acid 589-06-0 605-23-2, Ara-T

621-36-3, 3-Methylphenylacetic acid 622-47-9, 4-Methylphenylacetic acid

644-36-0, 2-Methylphenylacetic acid 1798-06-7, 4-Iodophenylacetic acid

1821-12-1, 4-Phenylbutyric acid 1878-65-5, 3-Chlorophenylacetic acid

1878-66-6, 4-Chlorophenylacetic acid 2444-36-2, 2-Chlorophenylacetic

acid 3056-17-5, d4T 3083-77-0, Ara-U 3416-05-5, 3'-Deoxythymidine

4097-22-7 4291-63-8, 2-Chloro-2'-deoxyadenosine 4619-18-5 5536-17-4,
Ara-A 5690-03-9, Splitomicin 6575-24-2, 2,6-Dichlorophenylacetic acid
7021-09-2, α -Methoxyphenylacetic acid 7057-48-9 7481-88-1, D4C
7481-89-2, DdC 15176-29-1, 5-Ethyl-2'-deoxyuridine 21679-14-1,
Fludarabine 22991-05-5 25526-93-6, FLT 27913-58-2 30516-87-1, AZT
36791-04-5, Ribavirin 38669-41-9, Phenoxypropionic acid 38669-42-0,
Phenoxybutyric acid 38819-10-2 39809-25-1, Penciclovir 41107-56-6
51246-79-8 53766-80-6 56045-73-9 59277-89-3, Aciclovir 66323-44-2
66323-46-4 68449-31-0 69123-98-4, 1-[2-Deoxy-2-fluoro- β -D-
arabinofuranosyl]-5-iodouracil 69256-17-3, FMAU 69304-47-8, BVDU
69655-05-6, DdI 77181-69-2, BVaraU 79637-79-9 79872-72-3
82410-32-0, Ganciclovir 84472-85-5, AzdU 84472-89-9 85236-92-6
85326-06-3 85326-07-4 86304-28-1, Buciclovir 87190-74-7 87190-79-2
87190-80-5 87190-84-9 87418-35-7 91969-06-1, Ara-M 92562-88-4
95058-81-4, DFdC 103882-87-7, 2'-Deoxy-2',2'-difluoroguanosine
104227-87-4, Famciclovir 105380-83-4 105784-82-5 106060-85-9
107036-62-4 107550-73-2 107550-76-5 108441-50-5
108441-51-6 108895-46-1 109881-25-6 110142-99-9 110143-10-7,
Lodenosine 111495-90-0 111495-95-5 111495-96-6 111495-98-8
111496-01-6 114248-23-6 114551-78-9 114753-53-6 115249-86-0
115913-79-6 119555-47-4, RO31-6840 119644-22-3 119644-23-4
120443-30-3, (-)-Carbovir 120503-30-2 120503-34-6 120503-35-7
120826-45-1 121353-93-3 123318-82-1 124832-26-4, Valacyclovir
124903-20-4 127492-31-3 130108-72-4, 4'-Azidothymidine 130108-73-5,
4'-Azido-2'-deoxyadenosine 130108-74-6, 4'-Azido-2'-deoxyguanosine
130108-75-7, 4'-Azido-2'-deoxyuridine 130108-76-8, 4'-Azido-2'-
deoxycytidine 130108-77-9, 4'-Azido-2'-deoxyinosine 130108-82-6,
4'-Azido-3'-deoxythymidine 131682-41-2 132235-73-5 132796-66-8
132796-67-9 132796-68-0 134379-77-4 134678-17-4, 3TC 135212-57-6
139418-97-6, 4'-Azido-5-chloro-2'-deoxyuridine 139888-11-2,
4'-Cyanothymidine 143491-54-7, FTC 143491-57-0, (-)-FTC 145416-37-1
145514-01-8, DXG 146726-77-4 160707-68-6 160707-69-7 160707-70-0
160707-71-1 160963-01-9 181377-89-9 181377-90-2 181785-84-2
192572-12-6

RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(comps. containing gap junction communication-enhancing aromatic acids and
nucleoside analog prodrugs for enhanced cancer therapy)

IT **107036-62-4**

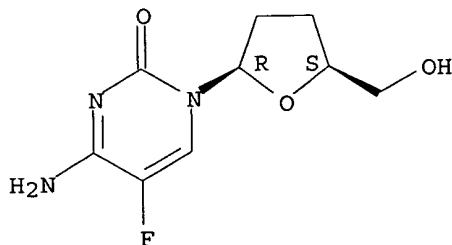
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(comps. containing gap junction communication-enhancing aromatic acids and
nucleoside analog prodrugs for enhanced cancer therapy)

RN 107036-62-4 HCAPLUS

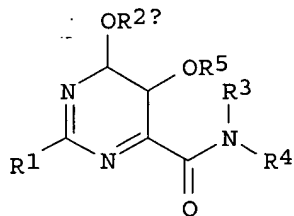
CN Cytidine, 2',3'-dideoxy-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

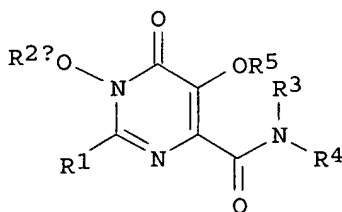


ACCESSION NUMBER: 2005:696887 HCAPLUS
DOCUMENT NUMBER: 143:194107
TITLE: Pyrimidyl phosphonate **antiviral** compounds
and methods of use
INVENTOR(S): Jin, Haolun; Kim, Choung U.
PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA
SOURCE: PCT Int. Appl., 170 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005070901	A2	20050804	WO 2005-US815	20050111
WO 2005070901	A3	20060504		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2005282839	A1	20051222	US 2005-33422	20050111
PRIORITY APPLN. INFO.:			US 2004-536010P	P 20040112
OTHER SOURCE(S):	MARPAT 143:194107			
GI				



I



II

AB Pyrimidine I and pyrimidinone II phosphonate compds. R1 = H, F, Cl, Br, I, OH, OR, NH2, ammonium, alkylamino, dialkylamino, trialkylammonium, carboxy, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, 4-dialkylaminopyridinium, alkyl sulfone, aryl sulfone, aryl sulfoxide, arylthio, sulfonamide, alkyl sulfoxide, formyl, ester, amido, 5-7 membered ring lactone, nitrile, azido, nitro, C1-18 alkyl, C1-18 substituted alkyl, C2-18 alkenyl, C2-C18 substituted alkenyl, C2-18 alkynyl, C2-18 substituted alkynyl, C6-20 aryl, C6-20 substituted aryl, C2-20 heterocycle, and C2-20 substituted heterocycle, phosphonate, phosphate, polyethyleneoxy, a protecting group, etc. R2a, R5 = independently selected from H, carboxy, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, 4-dialkylaminopyridinium, alkyl sulfone, aryl sulfone, aryl

sulfoxide, arylthio, sulfonamide, alkyl sulfoxide, formyl, ester, amido, 5-7 membered ring lactam, 5-7 membered ring lactone, nitrile, azido, nitro, C1-18 alkyl, C1-18 substituted alkyl, C2-18 alkenyl, C2-18 substituted alkenyl, C2-18 alkynyl, C2-18 substituted alkynyl, C6-20 aryl, C6-20 substituted aryl, C2-20 heterocycle, and C2-20 substituted heterocycle, phosphonate, phosphate, polyethyleneoxy, a protecting group, etc.; R2b, R3, R4 = H, OH, OR, amino, ammonium, alkylamino, dialkylamino, trialkylammonium, carboxy, sulfate, sulfamate, sulfonate, 5-7 membered ring sultam, 4-dialkylaminopyridinium, alkyl sulfone, aryl sulfone, aryl sulfoxide, arylthio, sulfonamide, alkyl sulfoxide, formyl, ester, amido, 5-7 membered ring lactam, 5-7 membered ring lactone, nitrile, azido, nitro, C1-18 alkyl, C1-18 substituted alkyl, C2-18 alkenyl, C2-18 substituted alkenyl, C2-18 alkynyl, C2-18 substituted alkynyl, C6-20 aryl, C6-20 substituted aryl, C2-20 heterocycle, and C2-20 substituted heterocycle, phosphonate, phosphate, polyethyleneoxy, a protecting group, etc.; and methods for viral inhibition are disclosed. The compds. include at least one phosphonate group covalently attached at any site.

IC ICM C07D239-54

ICS A61K031-513; A61P031-18

CC 29-7 (Organometallic and Organometalloidal Compounds)

Section cross-reference(s): 1, 33, 63

ST pyrimidyl phosphonate prepn **antiviral**

IT Anti-AIDS agents

Anti-infective agents

Antiviral agents

Immunomodulators

(preparation of pyrimidyl phosphonate **antiviral** compds. and methods of use)

IT 70-00-8, Trifluorothymidine 127-07-1, Hydroxyurea 320-67-2, 5-Azacytidine 961-07-9 2353-33-5, 5-Aza-2'-deoxycytidine 3056-17-5, Stavudine 4097-22-7, 2',3'-Dideoxyadenosine 4408-78-0, Phosphonoacetic acid 4428-95-9, Foscarnet 4546-70-7 5536-17-4, Vidarabine 7481-88-1, d4C 7481-89-2, Zalcitabine 21679-14-1, F-Ara-A 25526-93-6, FLT 30516-87-1, Retrovir 34079-68-0 36791-04-5, Ribavirin 38819-10-2 39809-25-1, Penciclovir 59277-89-3, Acyclovir 62488-57-7, 5,6-Dihydro-5-azacytidine 69123-90-6, FIAC 69123-98-4, FIAU 69256-17-3, FMAU 69304-47-8 69655-05-6, Videx 77181-69-2, BvaraU 78842-13-4 82410-32-0, Gancyclovir 83546-42-3, FEAU 86304-28-1, Buciclovir 92047-17-1, FL-G 92999-29-6, HPMMA 100018-53-9 103913-16-2, Oxetanocin A **107036-62-4** 107550-73-2 113269-46-8, Oxetanocin G 113852-37-2, Cidofovir 113852-41-8; PMEDAP 114987-19-8, Cytallene 121154-51-6 126062-18-8 127779-20-8, Saquinavir 129618-40-2, Nevirapine 130306-02-4, FMdC 134444-47-6 134678-17-4, Lamivudine 135212-57-6 135295-27-1 136470-78-5, Abacavir 136817-59-9, Delavirdine 137422-59-4 142217-69-4, BMS200475 142340-99-6, Adefovir dipivoxil 142632-32-4, Calanolide A 145417-33-0 145514-01-8 145514-04-1, Dapd 147127-20-6, PMPA 150378-17-9, Indinavir 154598-52-4, Efavirenz 155213-67-5, Ritonavir 159519-65-0, Enfuvirtide 159989-64-7, Nelfinavir 161814-49-9, Amprenavir 163252-36-6, Clevudine 178979-85-6, Capravirine 181785-84-2 192725-17-0, Lopinavir 379270-37-8, GS-7340 861674-34-2

RL: BCP (Biochemical process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)

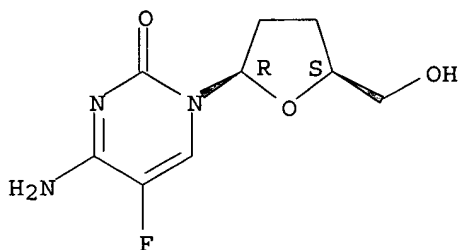
(preparation of pyrimidyl phosphonate **antiviral** compds. and methods of use)

IT 861674-31-9P 861674-33-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(preparation of pyrimidyl phosphonate **antiviral** compds. and methods of use)
IT 140-75-0, p-Fluorobenzylamine 67264-30-6 518047-36-4 861674-32-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pyrimidyl phosphonate **antiviral** compds. and methods of use)
IT 518047-35-3P 518047-69-3P 861674-29-5P 861674-30-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrimidyl phosphonate **antiviral** compds. and methods of use)
IT 107036-62-4
RL: BCP (Biochemical process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(preparation of pyrimidyl phosphonate **antiviral** compds. and methods of use)
RN 107036-62-4 HCAPLUS
CN Cytidine, 2',3'-dideoxy-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L69 ANSWER 4 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:965074 HCAPLUS
DOCUMENT NUMBER: 141:400969
TITLE: Preparation and therapeutic formulation of nucleoside phosphonate analogs as prodrugs in study of retention of therapeutic compounds inside cells
INVENTOR(S): Boojamara, Constantine G.; Chen, James M.; Chen, Xiaowu; Cho, Aesop; Chong, Lee S.; Fardis, Maria; Huang, Alan X.; Kim, Choung X.; Kirschberg, Thorsten A.; Lee, Christopher P.; Oare, David; Prasad, Vidya K.; Ray, Adrian S.; Swaminathan, Sundaramoorthi; Watkins, Will
PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA
SOURCE: PCT Int. Appl., 559 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 15
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096233	A2	20041111	WO 2004-US13060	20040426
WO 2004096233	A3	20050616		

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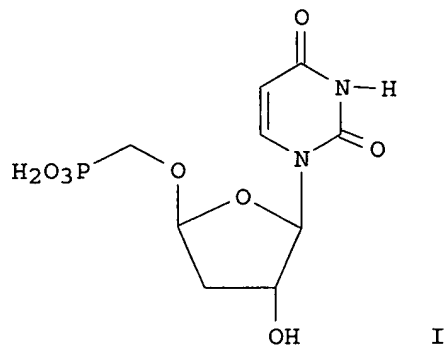
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CA 2523083	AA	20041111	CA 2004-2523083	20040426
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SN, TD, TG

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PRIORITY APPLN. INFO.:			US 2003-465347P	P 20030425
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US 2003-495317P	P	20030815
US 2003-495453P	P	20030815
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US 2003-495769P	P 20030815
US 2003-495772P	P 20030815
US 2003-495805P	P 20030815
US 2003-495964P	P 20030815



AB The invention is related to phosphorus substituted nucleoside compds. and therapeutic methods that include the administration of such compds., as well as to processes and intermediates useful for preparing such compds. The present invention relates to the accumulation or retention of therapeutic compds. inside cells (no data). The invention relates to attaining high concentration of phosphonate-containing nucleosides in target cells (no data).

Such

effective targeting may be applicable to a variety of combination chemotherapy, therapeutic formulation, and properties. Thus, nucleoside phosphonate I was prepared in study of retention of therapeutic compds. inside cells.

IC ICM A61K031-662

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1, 33

IT 951-77-9 3056-17-5 4291-63-8 30516-87-1, AZT 53910-25-1
55726-47-1 89458-19-5 95058-81-4 117176-51-9 120443-30-3
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126652-38-8 136470-78-5 141434-39-1 142217-69-4 **147058-39-7**
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790299-34-2 790299-35-3 790299-36-4 790299-37-5 790299-38-6
790299-39-7 790299-40-0 790299-41-1 790299-42-2 790299-43-3
790299-44-4 790299-45-5 790299-46-6

RL: BSU (Biological study, unclassified); **THU (Therapeutic use)**;

BIOL (Biological study); USES (Uses)

(preparation and therapeutic formulation of nucleoside phosphonate analogs as prodrugs in study of retention of therapeutic compds. inside cells)

IT **147058-39-7**

RL: BSU (Biological study, unclassified); **THU (Therapeutic use)**;

BIOL (Biological study); USES (Uses)

(preparation and therapeutic formulation of nucleoside phosphonate analogs as prodrugs in study of retention of therapeutic compds. inside cells)

RN 147058-39-7 HCAPLUS

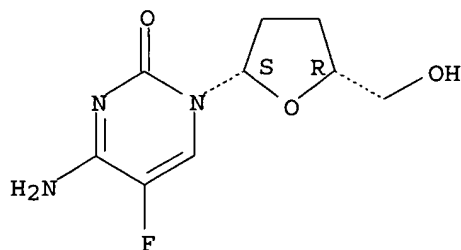
CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

US 2003-496416P	P 20030815
US 2003-510245P	P 20031010
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US 2003-513563P	P 20031024
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US 2003-513588P	P 20031024
US 2003-513589P	P 20031024
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US 2003-532230P	P 20031222
US 2003-532591P	P 20031223
US 2004-536005P	P 20040112

OTHER SOURCE(S) :
GI

MARPAT 141:400969



L69 ANSWER 5 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:41638 HCAPLUS

DOCUMENT NUMBER: 140:110132

TITLE: Allergic disease diagnosis and drug screening with TR3 and TINUR receptors

INVENTOR(S): Hashida, Ryoichi; Kagaya, Shinji; Sugita, Yuji; Saito, Hirohisa

PATENT ASSIGNEE(S): Genox Research, Inc., Japan; Japan as Represented by General Director of Agency of National Center for Child Health and Development

SOURCE: PCT Int. Appl., 158 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004005509	A1	20040115	WO 2003-JP8200	20030627
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003244132	A1	20040123	AU 2003-244132	20030627
US 2004214231	A1	20041028	US 2003-611310	20030701
PRIORITY APPLN. INFO.:			JP 2002-193841	A 20020702
			WO 2003-JP8200	W 20030627
AB Diagnosis of allergic diseases by measuring the expression level of orphan nuclear receptors TR3 and Nurrl (also known as NOT/TINUR/RNR-1/HZF-3), a member of the steroid/thyroid hormone nuclear receptor superfamily, or its encoding genes, and use of those receptors for screening of ligands usable as anti-allergic agents, are disclosed. Use of TR3 and TINUR receptors for inducing apoptosis is also claimed. Using differential display method, genes showing significantly increased expression in activated eosinophils of atopic dermatitis patients were identified. It was found that those genes coded for TR3 and TINUR receptors and is usable in diagnosis of and screening drug candidates for allergic diseases. A high throughput screening system constructed from modified mammalian two-hybrid screening was used to screen ligands for the TR3 and TINUR receptors. Prostaglandin (PGA) derivs. having cyclopentanone structure were				

identified as ligands and from those studies, actual effect of those compds. on the receptors was confirmed. Utilizing pharmacophore modeling, simulation of PGA derivative binding site for TR3 and TINUR receptors was carried out and compds. capable of binding to the receptors binding pocket were selected. It was also found that TR3 and TINUR expression was dramatically induced in peripheral blood eosinophils upon apoptosis stimulation with anti-CD30 antibodies having agonist activity toward CD30.

- IC ICM C12N015-09
ICS C07K014-47; C12Q001-02; C12Q001-68; A61K031-5575; A61K045-00;
A61P037-08; G01N033-15; G01N033-50; G01N033-53; G01N033-566;
A01K067-027
- CC 15-9 (Immunochemistry)
Section cross-reference(s): 1, 3, 9
- IT 61-74-5, Domoxin 76-58-4, Ethylmorphine 77-42-9, β -Santalol
90-41-5, 2-Aminobiphenyl 90-43-7, 2-Phenylphenol 90-52-8 91-04-3,
2,6-Dimethylol-4-methylphenol 99-48-9, Carveol 101-18-8,
3-Hydroxydiphenylamine 119-36-8, Methyl salicylate 119-42-6,
2-Cyclohexylphenol 119-53-9, Benzoin 129-24-8, Viridicatin 131-56-6,
Benzophenone-2,4-dihydroxy 134-20-3 134-37-2, Amphenidone 298-46-4,
Carbamazepine 304-88-1 428-07-9, Atromepine 441-38-3, Benzoinoxime
455-83-4, Dichlorophenarsine 473-67-6, Verbenol 482-28-0, Cinchonamine
499-75-2 500-92-5, Chloroguanide 500-99-2, 3,5-Dimethoxyphenol
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Benzophenoneoxime 579-45-3 582-33-2, 3-Aminobenzoic acid, ethyl ester
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butylphenol 1198-40-9, 4-Amino-7-chloroquinoline 1518-84-9,
Phenol-2-cyclopentyl 1565-39-5 1778-08-1, Salicylamide-N,N-dimethyl
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o-Methoxybenzamide 2565-54-0 2688-84-8, O-Phenoxyaniline 3035-45-8
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5363-33-7, Benzamide-O-butylamino 5579-06-6, Pentalamide 5983-08-4
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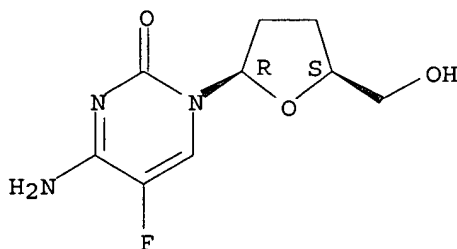
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119804-96-5, Dmdc 121353-93-3 121892-98-6 122568-02-9 122568-03-0
122568-04-1 122929-23-1 124583-48-8 132722-91-9 132722-92-0
132907-72-3, YM060 134379-77-4, RA 131423 134678-17-4, Lamivudine
134861-47-5 137500-42-6, Darsidomine
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(allergic disease diagnosis and drug screening with TR3 and TINUR
receptors)

IT 107036-62-4
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(allergic disease diagnosis and drug screening with TR3 and TINUR
receptors)

RN 107036-62-4 HCAPLUS

CN Cytidine, 2',3'-dideoxy-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L69 ANSWER 6 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:790092 HCAPLUS

DOCUMENT NUMBER: 136:144693

TITLE: Early detection of mixed mutations selected by
antiretroviral agents in HIV-infected primary human
lymphocytes

AUTHOR(S): Schinazi, Raymond F.; Schlueter-Wirtz, Susan; Stuyver,
Lieven

CORPORATE SOURCE: Department of Veterans Affairs, Decatur, GA, USA
SOURCE: Antiviral Chemistry & Chemotherapy (2001), 12(Suppl. 1), 61-65
CODEN: ACCHEH; ISSN: 0956-3202
PUBLISHER: International Medical Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A growing concern in the pursuit of new therapies for HIV-1 infection is the potential for the virus to develop drug resistance. With the advent of modern antiretroviral therapy and the common use of combined modalities, it is difficult to identify in the clinic the mutations associated with a specific drug. In general, drug selection of mutants using a relevant cell system, such as primary human lymphocytes, is a good prognosticator of what will happen in humans. In this study, HIV-infected human peripheral blood mononuclear cells were exposed, at a concentration of 1- to 10-fold the median effective **antiviral** concentration, to the nucleosides (-)- β -2',3'-dideoxy-3'-thia-5-fluorocytidine [(-)-FTC], (-)- β -2',3'-dideoxy-3'-thiacytidine (3TC), 3'-azido-2',3'-dideoxyuridine (CS-87, AZDU), 3'-azido-2',3'-dideoxy-5-methylcytidine (CS-92, AZMC), 2',3'-didehydro-3'-deoxythymidine (d4T), β -L-2',3'-didehydro-2',3'-dideoxy-5-fluorocytidine (β -L-D4FC), β -L-2',3'-dideoxyadenine SATE [β -L-ddAMP-bis(tbuty(SATE))], β -L-5-fluoro-2',3'-dideoxycytidine (L-FddC), and the protease inhibitors nelfinavir and amprenavir (VX-478). Virus from the culture supernatant was amplified by PCR and analyzed by both HIV-1 reverse transcriptase and protease line probe assay. All the L-nucleoside analogs tested selected for the V184 mutation, including the L-pyrimidine nucleosides 3TC (-)-FTC, β -L-FddC, β -L-D4FC and the β -L-purine nucleoside. β -L-D4FC also selected for K/R65 in addition to V184, indicating that these two mutations are linked and compatible in vitro. No pattern of mutations leading to resistance or reduced susceptibility was discerned with d4T. Rapid genotyping anal. revealed the different kinetics and mutations obtained by in vitro selection in HIV-infected cells exposed to nucleoside analogs and protease inhibitors.

CC 1-5 (Pharmacology)

IT Drug resistance

(**antiviral**; early detection of mixed mutations selected by antiretroviral agents in HIV-infected primary human lymphocytes)

IT **Antiviral** agents

Human immunodeficiency virus 1

Lymphocyte

Mutagens

(early detection of mixed mutations selected by antiretroviral agents in HIV-infected primary human lymphocytes)

IT 3056-17-5, d4T 84472-85-5, CS-87 87190-79-2, CS-92 134678-17-4, 3TC 143491-57-0, (-)-FTC **147058-39-7** 159989-64-7, Nelfinavir 161814-49-9, Amprenavir 181785-84-2 186648-57-7

RL: **PAC (Pharmacological activity)**; BIOL (Biological study)

(early detection of mixed mutations selected by antiretroviral agents in HIV-infected primary human lymphocytes)

IT **147058-39-7**

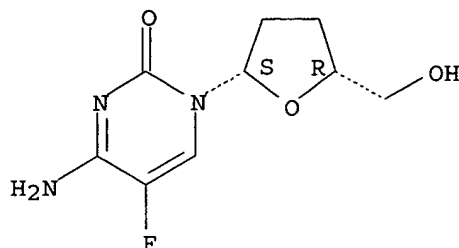
RL: **PAC (Pharmacological activity)**; BIOL (Biological study)

(early detection of mixed mutations selected by antiretroviral agents in HIV-infected primary human lymphocytes)

RN 147058-39-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L69 ANSWER 7 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:493737 HCAPLUS

DOCUMENT NUMBER: 135:227150

TITLE: Synthesis and evaluation of L-Fd4C and related nucleoside analogs as novel **antiviral** agents

AUTHOR(S): Chen, Shu-Hui

CORPORATE SOURCE: Vion Pharmaceuticals, Inc., New Haven, CT, 06511, USA

SOURCE: Frontiers of Biotechnology & Pharmaceuticals (2001), 2, 307-328
CODEN: FBPRBL

PUBLISHER: Science Press New York Ltd.

DOCUMENT TYPE: Journal; General Review

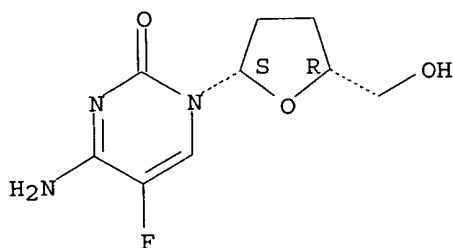
LANGUAGE: English

AB A review with 46 refs. The interest in L-nucleosides was spurred in recent years by the findings that L-nucleosides are generally endowed with lower host toxicity while maintaining good **antiviral** activity in comparison to their resp. D-nucleosides. The recent FDA approval of Lamivudine [L-BCH 189 (3TC)] for the treatment of HIV and HBV further supports these notions. Since the discovery of Lamivudine, a large number of 2',3'-dideoxy (dd)- and 2',3'-didehydro-2',3'-dideoxy (D4)-L-nucleoside analogs have been synthesized and evaluated in hopes of identifying even better **antiviral** agents. As a result, 2',3'-Dideoxy-2',3'-didehydro-beta-L-fluorocytidine (beta-L-Fd4C) was found to be a promising new lead. The first synthesis and **antiviral** activity assessment of L-Fd4C were reported by Lin and Cheng et al. in 1996. Recent disclosures from several labs. clearly demonstrated that L-Fd4C was the most potent anti-HBV agent reported to date (vs. 3TC, L-FddC, L-FMAU, etc.). In fact, L-Fd4C proved to be at least 10 times more potent than Lamivudine on HBV DNA synthesis in the hepatoma cell line HepG2 2.2.15. Compared with L-Fd4C, D-Fd4C showed similar anti-HIV activity yet reduced anti-HBV activity. 2'F-L-Fd4C exhibited excellent acid stability but reduced **antiviral** activity and cytotoxicity. Although L-Fd4C is converted intracellularly by cytoplasmic deoxycytidine kinase to its mono-, di- and triphosphate metabolites, the newly prepared bis(SATE)-L-Fd4CMP proved to be more potent against HBV yet less cytotoxic than L-Fd4C itself. The chemical synthesized L-Fd4CTP was found to be a poor substrate for human polymerase γ . A recent report from Zhu and Cheng et al. indicated that L-Fd4C had no inhibitory effect on mitochondrial DNA synthesis at concns. up to 10 μ M. An in vivo study involving HBV-infected ducks showed that longer administration of L-Fd4C induced a sustained suppression of viremia (>95%) and of viral DNA synthesis in the liver. The same study also demonstrated that L-Fd4C is more potent than 3TC in vivo. In summary, on the basis of the data

presented in this chapter, it is evident that L-Fd4C is endowed with exceptional anti-HBV activity (both in vitro and in vivo) as well as an acceptable toxicity profile, thus rendering it a very promising development candidate.

- CC 33-0 (Carbohydrates)
Section cross-reference(s): 1
- ST nucleoside lamivudine **antiviral** dideoxydidehydrobetafluorocytidine synthesis cytotoxicity review cytotoxicity
- IT **Antiviral** agents
Cytotoxicity
(synthesis and evaluation of L-Fd4C and related nucleoside analogs as novel **antiviral** agents)
- IT Nucleosides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); MSC (Miscellaneous); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and evaluation of L-Fd4C and related nucleoside analogs as novel **antiviral** agents)
- IT 134678-17-4P, Lamivudine **147058-39-7P** 163252-36-6P
181785-84-2P 203635-05-6P 209864-66-4P
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); MSC (Miscellaneous); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and evaluation of L-Fd4C and related nucleoside analogs as novel **antiviral** agents)
- IT **147058-39-7P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); MSC (Miscellaneous); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and evaluation of L-Fd4C and related nucleoside analogs as novel **antiviral** agents)
- RN 147058-39-7 HCAPLUS
- CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

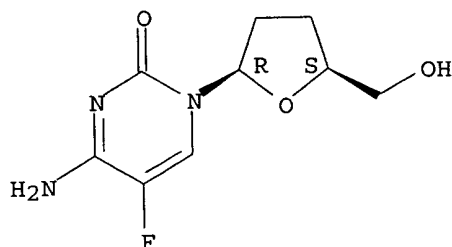


REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L69 ANSWER 8 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:780083 HCAPLUS
DOCUMENT NUMBER: 134:110094
TITLE: Anti-human immunodeficiency virus activities of nucleosides and nucleotides: correlation with molecular electrostatic potential data
AUTHOR(S): Mickel, Travis; Nair, Vasu
CORPORATE SOURCE: Department of Chemistry, The University of Iowa, Iowa

City, IA, 52242, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2000), 44(11),
2939-2947
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Examination of the anti-human immunodeficiency virus (HIV) data of some normal and isomeric dideoxynucleosides (ddNs and isoddNs), their three-dimensional (3-D) electron d. patterns, their electrostatic potential surfaces (EPS), and their conformational maps reveals some interesting correlations. For example, the EPS of (S,S)-isoddA shows regions of high and low electrostatic potential remarkably similar to those of β -D-3'-azido-3'-deoxythymidine (β -D-AZT), (-)-oxetanocin A, and (-)-carbovir. Such correlations involving EPS data and anti-HIV activity were also found with many other active nucleosides. Conversely, inactive compds. had EPS different from those of compds. in the same series that were active. For example, apio-ddNs, which are inactive against HIV, exhibit clear differences in electrostatic potential and 3-D electron d. shape from isoddNs that are active against HIV. Addnl., the inactivity of (S,S)-isoddC and (S,S)-isoddT can be correlated convincingly with a combination of their EPS data and their conformational energy maps. The electrostatic potential distributions of active nucleoside triphosphates show remarkable correlations. For example, (S,S)-isoddATP, AZT triphosphate (AZTTP), and oxetanocin A TP have similar 3-D electron d. surface patterns and similar high and low regions of electrostatic potential, which may suggest that these compds. proceed through related mechanisms in their interactions with, and inhibition of, HIV reverse transcriptase (RT). Docking of AZTTP, (S,S)-isoddATP, and other active triphosphates into the active site of HIV RT and calcn. of the EPS of both the nucleotide and the active site show that there is excellent matching between inhibitor and enzyme binding site EPS data. The structure-activity profile discovered has contributed to the development of a first predictive quant. structure-activity relation anal. in the area.
CC 1-3 (Pharmacology)
IT 7481-89-2 30516-87-1 51246-79-8 84472-85-5 84472-89-9 87190-80-5
103913-16-2 107036-62-4 108895-46-1 120443-30-3
127492-32-4 127682-75-1 134665-22-8 134678-17-4 143191-77-9
143191-82-6 143191-83-7 143288-99-7 143491-57-0 145416-37-1
145514-01-8 146609-00-9 160707-68-6 160707-69-7 160707-70-0
160707-71-1 160963-01-9 181377-89-9 181377-90-2 181785-84-2
192572-12-6
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(anti-human immunodeficiency virus activities of nucleosides and nucleotides, correlation with mol. electrostatic potential data)
IT 107036-62-4
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(anti-human immunodeficiency virus activities of nucleosides and nucleotides, correlation with mol. electrostatic potential data)
RN 107036-62-4 HCAPLUS
CN Cytidine, 2',3'-dideoxy-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L69 ANSWER 9 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:819251 HCAPLUS

DOCUMENT NUMBER: 132:59139

TITLE: Use of 3'-azido-2',3'-dideoxyuridine in combination with further anti-HIV drugs for the manufacture of a medicament for the treatment of HIV infection

INVENTOR(S): Schinazi, Raymond; Bryant, Martin L.; Myers, Maureen W.

PATENT ASSIGNEE(S): Emory University, USA; Novirio Pharmaceuticals Ltd.

SOURCE: PCT Int. Appl., 71 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9966936	A1	19991229	WO 1999-US14329	19990624
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2335617	AA	19991229	CA 1999-2335617	19990624
AU 9947162	A1	20000110	AU 1999-47162	19990624
US 6194391	B1	20010227	US 1999-339133	19990624
EP 1089741	A1	20010411	EP 1999-930672	19990624
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, RO			
BR 9911457	A	20011211	BR 1999-11457	19990624
US 2001009906	A1	20010726	US 2001-793346	20010226
US 6602664	B2	20030805		

PRIORITY APPLN. INFO.:

US 1998-90552P	P	19980624
US 1999-132126P	P	19990430
US 1999-339133	A1	19990624
WO 1999-US14329	W	19990624

AB It has been discovered that 3'-azido-2',3'-dideoxyuridine (CS-87) induces a transient mutation in HIV-1 at the 70th codon (K to R, i.e., lysine to arginine) of the reverse transcriptase region of the virus. Based on this discovery, a method and composition for treating HIV is provided that includes

administering CS-87 or its pharmaceutically acceptable salt or prodrug to a human in need of therapy in combination or alternation with a drug that induces a mutation in HIV-1 at a location other than the 70th codon of the reverse transcriptase region. This invention can be practiced by referring to the published mutation patterns for known anti-HIV drugs, or by determining the mutation pattern for a new drug.

IC ICM A61K031-70

CC 1-5 (Pharmacology)

Section cross-reference(s): 63

ST azidodideoxyuridine combination HIV **antiviral**; CS87 combination HIV **antiviral**; reverse transcriptase mutation HIV1 azidodideoxyuridine

IT **Antiviral** agents

Human immunodeficiency virus

Human immunodeficiency virus 1

(Use of 3'-azido-2',3'-dideoxyuridine in combination with further anti-HIV drugs for the manufacture of a medicament for the treatment of HIV)

IT 30516-87-1 69655-05-6, DdI 87190-79-2, CS 92 106941-25-7, Adefovir 110143-10-7, FddA 126502-08-7 127779-20-8, Saquinavir 129618-40-2, Nevirapine 134379-77-4 134678-17-4, 3TC 136470-78-5, Abacavir 136817-59-9, Delavirdine 143491-54-7, FTC 143491-57-0 **147058-39-7** 147127-20-6 149950-60-7, MKC-442 150378-17-9, Indinavir 154598-52-4, Efavirenz 155213-67-5, Ritonavir 159989-64-7, Nelfinavir 161814-49-9, Amprenavir 178979-85-6 181785-84-2 **181785-87-5D**, isomers 192725-17-0, ABT-378 253199-05-2, JPS 783 253199-06-3, NV 01

RL: **BAC (Biological activity or effector, except adverse)**; BSU

(Biological study, unclassified); **THU (Therapeutic use)**; BIOL

(Biological study); USES (Uses)

(azidodideoxyuridine in combination with other anti-HIV drugs for treatment of HIV infection)

IT **147058-39-7 181785-87-5D**, isomers

RL: **BAC (Biological activity or effector, except adverse)**; BSU

(Biological study, unclassified); **THU (Therapeutic use)**; BIOL

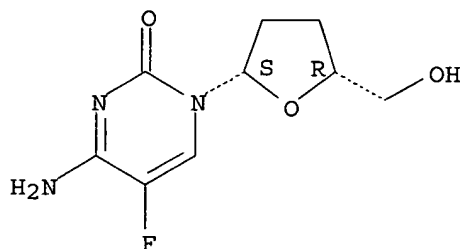
(Biological study); USES (Uses)

(azidodideoxyuridine in combination with other anti-HIV drugs for treatment of HIV infection)

RN 147058-39-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

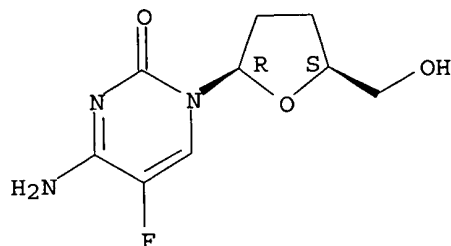
Absolute stereochemistry. Rotation (-).



RN 181785-87-5 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2R,5S)-tetrahydro-5-(hydroxymethyl)-2-furanyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L69 ANSWER 10 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:594332 HCAPLUS

DOCUMENT NUMBER: 131:317318

TITLE: QSAR studies of **antiviral** agents using molecular similarity analysis and structure-activity maps

AUTHOR(S): Parakulam, R. R.; Lesniewski, M. L.; Taylor-McCabe, K. J.; Tsai, C.

CORPORATE SOURCE: Department of Chemistry, Kent State University, Kent, OH, 44242-0001, USA

SOURCE: SAR and QSAR in Environmental Research (1999), 10(2-3), 175-206

CODEN: SQERED; ISSN: 1062-936X

PUBLISHER: Gordon & Breach Science Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Quant. structure-activity relationships (QSAR) were developed for nucleoside analogs with anti-HIV activity. These compds. were investigated to determine the correlation of structure and toxicity/activity using mol. similarity anal. and structure-activity maps. A multiple-formula approach was used to perform quant. mol. similarity anal. (QMSA) and QSAR study. Mol. descriptors such as number of atoms and bonds of a mol. (NAB), maximum common substructure (MaCS), and mol. similarity index (MSI) were used in the authors structure-activity relation study. The MaCS of two mols. is defined as the substructure with the greatest NAB value common to both mols. The MSI of two mols. X and Y is defined as $MSI(X,Y) = [MaCS(X,Y)/NAB(X)] + [MaCS(X,Y)/NAB(Y)]$. MaCS and MSI quantify the similarity between two mol. structures. Structure-activity maps (structure-toxicity map and structure-**antiviral** map) and QMSA were used to determine the site and type of modification for reduced toxicity and improved activity of new compds.

CC 1-3 (Pharmacology)

ST QSAR **antiviral** pyrimidine nucleoside analog toxicity

IT **Antiviral** agents

Human immunodeficiency virus 1

QSAR (structure-activity relationship)

(QSAR studies of **antiviral** pyrimidine nucleoside analogs with anti-HIV activity in relation to toxicity using mol. similarity anal. and structure-activity maps)

IT Pyrimidine nucleosides

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(QSAR studies of **antiviral** pyrimidine nucleoside analogs with

anti-HIV activity in relation to toxicity using mol. similarity anal. and structure-activity maps)

IT Structure-activity relationship

(**antiviral**; QSAR studies of **antiviral** pyrimidine nucleoside analogs with anti-HIV activity in relation to toxicity using mol. similarity anal. and structure-activity maps)

IT Toxicity

(drug; QSAR studies of **antiviral** pyrimidine nucleoside analogs with anti-HIV activity in relation to toxicity using mol. similarity anal. and structure-activity maps)

IT 3056-17-5 3416-05-5, Thymidine 3'-deoxy- 5974-93-6 5983-09-5
7481-88-1 7481-89-2 25526-93-6 30516-87-1 41107-55-5 51246-79-8
73149-33-4 80647-03-6 84472-85-5 84472-89-9 87190-79-2
108441-51-6, Uridine, 3'-azido-5-chloro-2',3'-dideoxy- 108895-49-4
108895-53-0 115249-86-0 115249-95-1 115913-78-5 115913-83-2
115913-85-4 116195-58-5 117174-38-6 118222-08-5 119555-47-4
119644-22-3 119644-23-4, Uridine, 2',3'-dideoxy-3'-fluoro-5-iodo-
120815-05-6 121353-87-5 121353-89-7 121353-93-3 121354-03-8
121372-82-5 124743-30-2 **124743-31-3** 124903-20-4
125217-37-0, Uridine, 3'-deoxy-3'-fluoro-5-methyl- 127492-31-3
127492-32-4, Cytidine, 5-chloro-2',3'-dideoxy-3'-fluoro- 127592-40-9
127840-99-7 127841-03-6 130351-55-2 134680-32-3 248959-86-6
248959-87-7 248959-88-8 248959-89-9 248959-90-2

RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(QSAR studies of **antiviral** pyrimidine nucleoside analogs with anti-HIV activity in relation to toxicity using mol. similarity anal. and structure-activity maps)

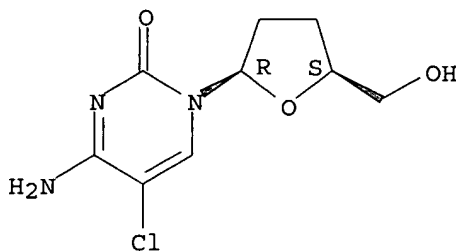
IT **124743-31-3**

RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(QSAR studies of **antiviral** pyrimidine nucleoside analogs with anti-HIV activity in relation to toxicity using mol. similarity anal. and structure-activity maps)

RN 124743-31-3 HCAPLUS

CN Cytidine, 5-chloro-2',3'-dideoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L69 ANSWER 11 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:436510 HCAPLUS

DOCUMENT NUMBER: 129:183832

TITLE: Metabolism of 2',3'-dideoxy-2',3'-didehydro-β-L(-

) -5-fluorocytidine and its activity in combination with clinically approved anti-human immunodeficiency virus β -D(+) nucleoside analogs in vitro

AUTHOR(S): Dutschman, Ginger E.; Bridges, Edward G.; Liu, Shwu-Huey; Gullen, Elizabeth; Guo, Xin; Kukhanova, Marina; Cheng, Yung-Chi

CORPORATE SOURCE: Department Pharmacology, Yale University School Medicine, New Haven, CT, 06520, USA

SOURCE: Antimicrobial Agents and Chemotherapy (1998), 42(7), 1799-1804

CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 2',3'-Dideoxy-2',3'-didehydro- β -L(-)-5-fluorocytidine [L(-)Fd4C] has been reported to be a potent inhibitor of the human immunodeficiency virus (HIV) in cell culture. In the present study the **antiviral** activity of this compound in two-drug combinations and its intracellular metabolism are addressed. The two-drug combination of L(-)Fd4C plus 2',3'-didehydro-2',3'-dideoxythymidine (D4T, or stavudine) or 3'-azido-3'-deoxythymidine (AZT, or zidovudine) synergistically inhibited replication of HIV in vitro. Additive **antiviral** activity was observed with L(-)Fd4C in combination with 2',3'-dideoxycytidine (ddC, or zalcitabine) or 2',3'-dideoxyinosine (ddI, or didanosine). This β -L(-) nucleoside analog has no activity against mitochondrial DNA synthesis at concns. up to 10 μ M. As it was previously reported for other β -L(-) nucleoside analogs, L(-)Fd4C could protect against mitochondrial toxicity associated with D4T, ddC, and ddI. Metabolism studies showed that this drug is converted intracellularly to its mono-, di-, and triphosphate metabolites. The enzyme responsible for monophosphate formation was identified as cytoplasmic deoxycytidine kinase, and the K_m is 100 μ M. L(-)Fd4C was not recognized in vitro by human mitochondrial deoxypyrimidine nucleoside kinase. Also, L(-)Fd4C was not a substrate for deoxycytidine deaminase. L(-)Fd4C 5'-triphosphate served as an alternative substrate to dCTP for incorporation into DNA by HIV reverse transcriptase. The favorable anti-HIV activity and protection from mitochondrial toxicity by L(-)Fd4C in two-drug combinations favors the further development of L(-)Fd4C as an anti-HIV agent.

CC 1-2 (Pharmacology)

Section cross-reference(s): 10

ST dideoxydidehydrofluorocytidine AZT pharmacokinetics HIV nucleoside **antiviral**

IT **Antiviral** agents
DNA formation
Drug interactions
Drug metabolism
Human immunodeficiency virus 1
Mitochondria
Phosphorylation, biological
(metabolism of dideoxydidehydrofluorocytidine and its activity in combination with anti-HIV nucleoside analogs in vitro)

IT 3056-17-5, D4T 7481-89-2, DdC 30516-87-1, AZT 69655-05-6, DdI 134678-17-4 135212-57-6 147058-39-7

RL: **BAC** (**B**iological **a**ctivity or **e**ffector, **e**xcept **a**dverse); **BSU** (**B**iological study, **u**nclassified); **THU** (**T**herapeutic **u**se); **BIOL** (**B**iological study); **USES** (**U**ses)
(metabolism of dideoxydidehydrofluorocytidine and its activity in combination with anti-HIV nucleoside analogs in vitro)

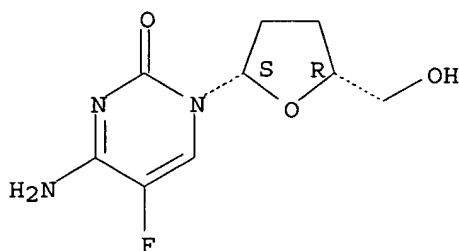
IT 147058-39-7

RL: **BAC** (**Biological activity or effector, except adverse**); BSU
(Biological study, unclassified); **THU** (**Therapeutic use**); BIOL
(Biological study); USES (Uses)
(metabolism of dideoxydidehydrofluorocytidine and its activity in
combination with anti-HIV nucleoside analogs in vitro)

RN 147058-39-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-
(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L69 ANSWER 12 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:392087 HCAPLUS

DOCUMENT NUMBER: 129:36433

TITLE: Method for reducing toxicity of D-nucleoside analogs
with L-nucleosides

INVENTOR(S): Cheng, Yung-chi; Lin, Tai-shun

PATENT ASSIGNEE(S): Yale University, USA

SOURCE: U.S., 14 pp., Cont.-in-part of U. S. Ser. No. 406,198.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	---	-----	-----	-----
US 5756478	A	19980526	US 1996-616912	19960315
US 5869461	A	19990209	US 1995-406198	19950316
PRIORITY APPLN. INFO.:			US 1995-406198	A2 19950316

AB The present invention relates to novel methods for reducing toxicity
associated with the administration of conventional D-nucleoside compds.,
including anti-HIV nucleosides and related therapeutic agents.
Therapeutic D-nucleosides exhibit unexpectedly reduced toxicity when
coadministered with effective amts. of L-nucleoside compds. The method
are particularly useful for the treatment of HIV infections and
AIDS-related symptoms in humans. Thus, coadministration of
 β -L-5-fluoro-2',3'-dideoxycytidine inhibited the ability of AZT, ddC,
ddI, and D4T to inhibit mitochondrial DNA synthesis in CEM cells and
decreased the anti-HIV ID50 of these compds.

IC ICM A61K031-70

ICS C07H019-073; C07H019-173

INCL 514045000

CC 1-5 (Pharmacology)

IT **Antiviral agents**

(reducing toxicity of D-nucleoside analogs by coadministration of L-nucleosides)

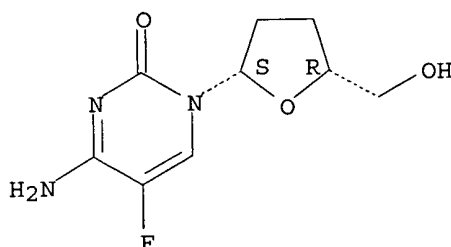
IT 121154-51-6, β -L-2',3'-Dideoxycytidine 134678-17-4 135212-57-6
143491-57-0 147058-39-7 181785-84-2
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); BIOL (Biological study)
(reducing toxicity of D-nucleoside analogs by coadministration of L-nucleosides)

IT 147058-39-7
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); BIOL (Biological study)
(reducing toxicity of D-nucleoside analogs by coadministration of L-nucleosides)

RN 147058-39-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L69 ANSWER 13 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:350076 HCAPLUS

DOCUMENT NUMBER: 129:103801

TITLE: Interaction of β -L-2',3'-dideoxy-2',3'-didehydro-5-fluoro-CTP with human immunodeficiency virus-1 reverse transcriptase and human DNA polymerases: implications for human immunodeficiency virus drug design

AUTHOR(S): Kukhanova, Marina; Li, Xiuyan; Chen, Shu-Hui; King, Ivan; Doyle, Terrence; Prusoff, William; Cheng, Yung-Chi

CORPORATE SOURCE: Department of Pharmacology, Yale University School of Medicine, New Haven, CT, 06510, USA

SOURCE: Molecular Pharmacology (1998), 53(5), 801-807

CODEN: MOPMA3; ISSN: 0026-895X

PUBLISHER: Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The work reported in this article has evaluated the relative mol. activity of the 5'-triphosphate of a novel β -L-nucleoside with an unsatd. ribose residue, β -L-2',3'-dideoxy-2',3'-didehydro-5-fluorocytidine (β -L-Fd4CTP), with that of β -L-2',3'-dideoxy-5-fluorocytidine (β -L-FddCTP) and 2',3'-dideoxycytidine (ddCTP), on DNA strand elongation by human immunodeficiency virus-1 reverse transcriptase (HIV RT) and human DNA polymerases α (pol α), β (pol β), γ (pol γ) and ϵ (pol ϵ). The concns. of

β -L-Fd4CTP that inhibited the yield of products by 50% were 0.20 μ M, 1.8 μ M, and 4.0 μ M for HIV RT, pol γ , and pol β , resp. The β -L-Fd4CTP at a concentration as high as 40 μ M had no inhibitory effect on pol ϵ , but could inhibit pol α by 10-20% at 20 μ M. The K_m and relative V_{max} values of β -L-Fd4CTP, β -L-FddCTP, and ddCTP for incorporation into the standing start point of 5'-[32P]-oligonucleotide primer annealed with M13mp19 phage DNA by HIV RT and human DNA polymerases were evaluated. The efficiency of incorporation (V_{max}/K_m) of β -L-Fd4CTP by HIV RT was about 4-fold and 12-fold higher than that of ddCTP and β -L-FddCTP, resp. In contrast, the V_{max}/K_m ratio of β -L-Fd4CTP for pol γ was 7-fold lower than that of ddCTP, but 4-fold higher than that of β -L-FddCTP. Pol α could use β -L-Fd4CTP as a substrate, but only at a high concentration (>20 μ M). Incorporation of β -L-Fd4CTP by pol ϵ could not be detected. A hypothesis about the preferable recognition of the 2',3'-dideoxy-2',3'-didehydro- structure of β -L-Fd4CTP to that of the 2',3'-dideoxy-structure of β -L-FddCTP by HIV RT is discussed.

CC 1-5 (Pharmacology)

IT 66004-77-1, DdCTP 161170-31-6

RL: **BAC** (*Biological activity or effector, except adverse*); BSU (Biological study, unclassified); **THU** (*Therapeutic use*); BIOL (Biological study); USES (Uses)

(interaction of β -L-2',3'-dideoxy-2',3'-didehydro-5-fluoro-CTP with HIV-1 reverse transcriptase and human DNA polymerases: implications for HIV drug design)

IT 161170-31-6

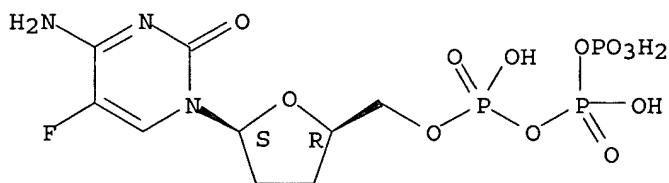
RL: **BAC** (*Biological activity or effector, except adverse*); BSU (Biological study, unclassified); **THU** (*Therapeutic use*); BIOL (Biological study); USES (Uses)

(interaction of β -L-2',3'-dideoxy-2',3'-didehydro-5-fluoro-CTP with HIV-1 reverse transcriptase and human DNA polymerases: implications for HIV drug design)

RN 161170-31-6 HCAPLUS

CN Triphosphoric acid, P-[(2R,5S)-[5-(4-amino-5-fluoro-2-oxo-1(2H)-pyrimidinyl)tetrahydro-2-furanyl]methyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L69 ANSWER 14 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:294458 HCAPLUS

DOCUMENT NUMBER: 129:51283

TITLE: Chiral influences of feedback inhibition with dCTP on murine deoxycytidine kinase

AUTHOR(S): Tomikawa, Aki; Yamaguchi, Toyofumi; Kawaguchi, Takeo; Shudo, Koichi; Saneyoshi, Mineo

CORPORATE SOURCE: Dep. of Biological Sciences, Teikyo University of Science and Technology, Yamanashi, 409-01, Japan

SOURCE: Nucleic Acids Symposium Series (1997), 37 (Symposium on Nucleic Acids Chemistry, 1997), 181-182
CODEN: NACSD8; ISSN: 0261-3166

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The inhibitory effects of 4 kinds of 2'-deoxy-L-nucleoside 5'-triphosphates, which are enantiomers of natural dNTPs, on murine deoxycytidine kinase (dCK) were investigated. When ATP was used as the phosphate donor, L-dCTP showed significant inhibitory action noncompetitively and competitively with 2'-deoxycytidine (dCyd) and ATP, resp. Thus L-dCTP, like dCTP, could serve as a feedback inhibitor of dCK. Recently, it has been demonstrated that human dCK can utilize L-dCyd as a substrate (Verri, A. et al. (1997) Mol. Pharmacol., 51, 132). The present results suggest that dCK is also unable to discriminate the chirality of nucleotides at the phosphate donor binding site of the enzyme.

CC 7-3 (Enzymes)

IT 2056-98-6, DCTP 121154-51-6 136891-12-8, BCH 189 143491-54-7, FTC 145918-75-8 **147058-39-7** 152502-95-9 189639-16-5 198632-86-9 198639-09-7

RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(chiral influences of feedback inhibition with dCTP on murine deoxycytidine kinase)

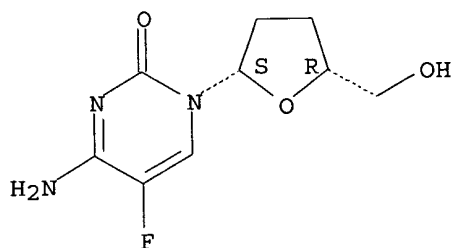
IT **147058-39-7**

RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(chiral influences of feedback inhibition with dCTP on murine deoxycytidine kinase)

RN 147058-39-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L69 ANSWER 15 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:64015 HCAPLUS

DOCUMENT NUMBER: 126:180842

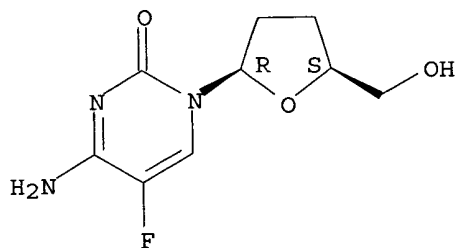
TITLE: Lack of enantiospecificity of human 2'-deoxycytidine kinase: relevance for the activation of β -L-deoxycytidine analogs as antineoplastic and **antiviral** agents

AUTHOR(S): Verri, Annalisa; Focher, Federico; Priori, Giuseppina;

Gosselin, Gilles; Imbach, Jean-Louis; Capobianco, Massimo; Garbesi, Anna; Spadari, Silvio
CORPORATE SOURCE: Istituto di Genetica Biochimica ed Evoluzionistica, Consiglio Nazionale delle Ricerche, Pavia, I-27100, Italy
SOURCE: Molecular Pharmacology (1997), 51(1), 132-138
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors demonstrate that human 2'-deoxycytidine kinase (dCK) is a nonenantioselective enzyme because it phosphorylates β -D-2'-deoxycytidine (D-dCyd), the natural substrate, and β -L-2'-deoxycytidine (L-dCyd), its enantiomer, with the same efficiency. Kinetic studies showed that L-dCyd is a competitive inhibitor of the phosphorylation of D-dCyd with a K_i value of 0.12 μ M, which is lower than the K_m value for D-dCyd (1.2 μ M). Chemical modification of either the base or the pentose ring strongly decreases the inhibitory potency of L-dCyd. L-dCyd is resistant to cytidine deaminase and competes in cell cultures with the natural D-dCyd as substrate for dCK, thus reducing the incorporation of exogenous [3 H]dCyd into DNA. L-dCyd had no effect on the pool of dTTP deriving from the salvage or from the de novo synthesis, does not inhibit short term RNA and protein syntheses, and shows little or no cytotoxicity. The results indicate a catalytic similarity between human dCK and herpetic thymidine kinases, enzymes that also lack stereospecificity. This functional analogy underlines the potential role of dCK as activator of L-deoxycytidine analogs as **antiviral** and antineoplastic agents and lends support to the hypothesis that herpesvirus thymidine kinase might have evolved from a captured cellular dCK gene, developing the ability to phosphorylate thymidine and retaining that to phosphorylate deoxycytidine.
CC 1-5 (Pharmacology)
Section cross-reference(s): 7
ST deoxycytidine kinase enantiospecificity analog antineoplastic **antiviral**
IT Antitumor agents
 Antiviral agents
 Enzyme kinetics
 Michaelis constant
 (lack of enantiospecificity of human 2'-deoxycytidine kinase and relevance for activation of β -L-deoxycytidine analogs as antineoplastic and **antiviral** agents in relation to cytidine deaminase and DNA formation and effect on cell growth)
IT 951-77-9 9039-45-6, 2'-Deoxycytidine kinase 40093-94-5
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (lack of enantiospecificity of human 2'-deoxycytidine kinase and relevance for activation of β -L-deoxycytidine analogs as antineoplastic and **antiviral** agents in relation to cytidine deaminase and DNA formation and effect on cell growth)
IT 3424-98-4 4449-40-5 7481-89-2 9025-06-3, Cytidine deaminase 14365-45-8 22837-44-1 31501-19-6 **107036-62-4** 121154-51-6 **147058-39-7** 154568-81-7 162239-35-2 166735-83-7 187467-31-8
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
 (lack of enantiospecificity of human 2'-deoxycytidine kinase and relevance for activation of β -L-deoxycytidine analogs as

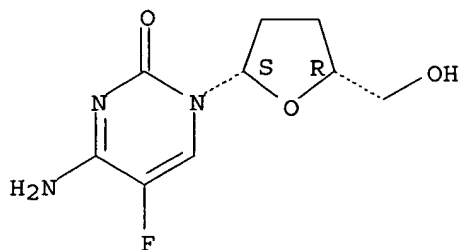
- antineoplastic and **antiviral** agents in relation to cytidine deaminase and DNA formation and effect on cell growth)
- IT 958-09-8, 2'-Deoxyadenosine 961-07-9, 2'-Deoxyguanosine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(lack of enantiospecificity of human 2'-deoxycytidine kinase and relevance for activation of β -L-deoxycytidine analogs as antineoplastic and **antiviral** agents in relation to cytidine deaminase and DNA formation and effect on cell growth)
- IT 1032-65-1
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(lack of enantiospecificity of human 2'-deoxycytidine kinase and relevance for activation of β -L-deoxycytidine analogs as antineoplastic and **antiviral** agents in relation to cytidine deaminase and DNA formation and effect on cell growth)
- IT 96744-89-7
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(lack of enantiospecificity of human 2'-deoxycytidine kinase and relevance for activation of β -L-deoxycytidine analogs as antineoplastic and **antiviral** agents in relation to cytidine deaminase and DNA formation and effect on cell growth)
- IT 107036-62-4 147058-39-7
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(lack of enantiospecificity of human 2'-deoxycytidine kinase and relevance for activation of β -L-deoxycytidine analogs as antineoplastic and **antiviral** agents in relation to cytidine deaminase and DNA formation and effect on cell growth)
- RN 107036-62-4 HCAPLUS
CN Cytidine, 2',3'-dideoxy-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



- RN 147058-39-7 HCAPLUS
CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L69 ANSWER 16 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:240715 HCAPLUS

DOCUMENT NUMBER: 124:306640

TITLE: Effects of nucleotide analogs on human immunodeficiency virus type 1 integrase

AUTHOR(S): Mazumder, Abhijit; Neamati, Nouri; Sommadossi, Jean-Pierre; Gosselin, Gilles; Schinazi, Raymond F.; Imbach, Jean-Louis; Pommier, Yves

CORPORATE SOURCE: Laboratory Molecular Pharmacology, National Cancer Institute, Bethesda, MD, 20892, USA

SOURCE: Molecular Pharmacology (1996), 49(4), 621-8
CODEN: MOPMA3; ISSN: 0026-895X

PUBLISHER: Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We extended our previous study with 3'-azido-3'-deoxythymidine nucleotides [Proc. Natl. Acad. Sci. USA 91:5771-5775 (1994)] and examined the effects on human immunodeficiency virus type 1 (HIV-1) integrase of the nucleotides of three nucleoside analogs currently under evaluation in clin. trials: β -D-2',3'-didehydro-3'-deoxythymidine, β -D-2'-ara-fluoro-2',3'-dideoxyadenosine, and β -L-2',3'-dideoxy-3'-thiacytidine. β -D-2',3'-Didehydro-3'-deoxythymidine and β -D-2'-ara-fluoro-2',3'-dideoxyadenosine nucleotides had IC₅₀ values for strand transfer of 100 and 200 μ M, resp., whereas the corresponding 2',3'-dideoxynucleoside triphosphates, ddT triphosphate and ddA triphosphate, did not inhibit the integrase at 800 and 200 μ M, resp. β -L-2',3'-Dideoxy-3'-thiacytidine triphosphate had no effect up to 500 μ M. The L-enantiomers of 5-fluoro-2',3'-dideoxycytidine monophosphate and triphosphate had IC₅₀ values of .apprx.40 μ M, whereas their D-enantiomer isomers showed no inhibition at 200 μ M. NAD, pyridoxal phosphate and coumermycin A1, which exhibit no **antiviral** activity but are typically used to probe nucleotide binding sites, were also tested. NAD was inactive, and its etheno derivative exhibited activity at 1 mM. In contrast, pyridoxal phosphate (IC₅₀ = 18 μ M) and coumermycin A1 (IC₅₀ = 5 μ M) were potent inhibitors. None of the coumermycin monomeric derivs. were active integrase inhibitors. The physiol. ribonucleotides ATP and GTP inhibited HIV-1 integrase at or near cellular concns., suggesting that they may regulate HIV-1 integrase activity in cells. In general, the active nucleotides tested inhibited binding of HIV-1 integrase to its substrate DNA and inhibited an integrase deletion mutant containing only amino acids 50-212, indicating that nucleotides bind to the enzyme catalytic core. Consistently, the choice of nucleophile in the 3'-processing reaction was blocked to the same extent regardless of the nucleotide used (water, glycerol, or the viral DNA hydroxyl) by the enzyme. These observations suggest new strategies

for **antiviral** drug development that could be based on nucleotide analogs as inhibitors of HIV-1 integrase.

CC 1-5 (Pharmacology)

Section cross-reference(s): 3, 7

IT 3056-17-5D, nucleotides 110143-10-7D, nucleotides 161170-31-6
170554-57-1

RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); USES (Uses)

(inhibition of HIV-1 integrase by; nucleotide analog inhibitors of
integrase of HIV-1)

IT 161170-31-6

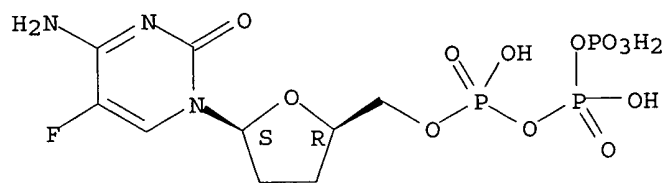
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); USES (Uses)

(inhibition of HIV-1 integrase by; nucleotide analog inhibitors of
integrase of HIV-1)

RN 161170-31-6 HCAPLUS

CN Triphosphoric acid, P-[(2R,5S)-[5-(4-amino-5-fluoro-2-oxo-1(2H)-
pyrimidinyl)tetrahydro-2-furanyl)methyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L69 ANSWER 17 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:176478 HCAPLUS

DOCUMENT NUMBER: 124:278075

TITLE: Favorable interaction of β -L(-)-nucleoside
analogs with clinically approved anti-HIV nucleoside
analogs for the treatment of human immunodeficiency
virus

AUTHOR(S): Bridges, Edward G.; Dutschman, Ginger E.; Gullen,
Elizabeth A.; Cheng, Yung-Chi

CORPORATE SOURCE: Dep. Pharmacology, Yale Univ. School Medicine, New
Haven, CT, 06510, USA

SOURCE: Biochemical Pharmacology (1996), 51(6), 731-6
CODEN: BCPA6; ISSN: 0006-2952

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The combination of (-)-2',3'-dideoxy-3'-thiacytidine (L(-)SddC, 3TC),
L(-)-2',3'-dideoxy-5-fluorocytidine (L(-)FddC), or L(-)-2',3'-dideoxy-5-
fluoro-3'-thiacytidine (L(-)FTC) with 3'-azido-3'-deoxythymidine (AZT)
synergistically inhibited replication of human immunodeficiency virus
(HIV) in vitro. Similar synergistic activity was also obtained when these
compds. were used in combination with 2',3'-didehydro-2',3'-
dideoxythymidine (D4T). In terms of 2',3'-dideoxyinosine (ddI) and
2',3'-dideoxycytidine (ddC), only additive anti-HIV activity was observed
None of the β -L(-)-nucleoside analogs had additive toxicity in cell
culture, and they could protect against the delayed mitochondrial toxicity

associated with AZT, D4T, ddC, and ddI in drug-treated cells. Thus, combinations of β -L(-) nucleoside analogs with any of the approved anti-HIV drugs could have a potentially beneficial outcome.

CC 1-5 (Pharmacology)

ST human immunodeficiency virus **antiviral** nucleoside analog; HIV **antiviral** nucleoside analog

IT 3056-17-5 7481-89-2, 2',3'-Dideoxycytidine 30516-87-1,
3'-Azido-3'-deoxythymidine 69655-05-6, 2',3'-Dideoxyinosine
134678-17-4, (-)-2',3'-Dideoxy-3'-thiacytidine 143491-57-0,
L(-)-2',3'-Ideoxy-5-fluoro-3'-thiacytidine **147058-39-7**

RL: ADV (Adverse effect, including toxicity); **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study);
USES (Uses)

(β -L-(-)-nucleoside analog interaction with clin. approved anti-HIV nucleoside analogs for the treatment of human immunodeficiency virus)

IT **147058-39-7**

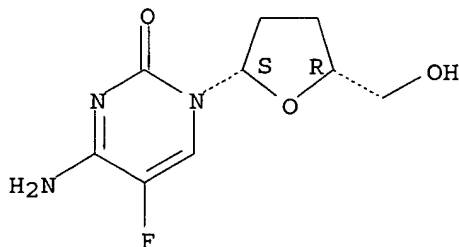
RL: ADV (Adverse effect, including toxicity); **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study);
USES (Uses)

(β -L-(-)-nucleoside analog interaction with clin. approved anti-HIV nucleoside analogs for the treatment of human immunodeficiency virus)

RN 147058-39-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L69 ANSWER 18 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:874681 HCAPLUS

DOCUMENT NUMBER: 123:286530

TITLE: synthesis of 2',3'-dideoxy- β -L-pentafuranonucleosides as virucides

INVENTOR(S): Gosselin, Gilles; Imbach, Jean-Louis; Aubertin, Anne-Marie; Sommadossi, Jean-Pierre; Schinazi, Raymond F.

PATENT ASSIGNEE(S): Center National de la Recherche-Scientifique (CNRS), Fr.

SOURCE: PCT Int. Appl., 34 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

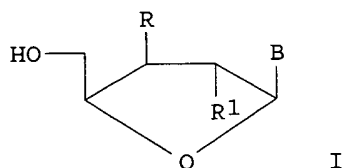
LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9507287	A1	19950316	WO 1994-FR1066	19940909
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2709754	A1	19950317	FR 1993-10798	19930910
FR 2709754	B1	19951201		
EP 717748	A1	19960626	EP 1994-926973	19940909
EP 717748	B1	19971217		
R: DE, FR, GB				
US 2002120130	A1	20020829	US 2001-953187	20010914
US 2005101776	A1	20050512	US 2003-672585	20030926
PRIORITY APPLN. INFO.:			FR 1993-10798	A 19930910
			WO 1994-FR1066	W 19940909
			US 1997-612965	B1 19970729
			US 2001-953187	B1 20010914

OTHER SOURCE(S): MARPAT 123:286530
GI



AB 2',3'-Dideoxy- β -L-pentafuranonucleosides I (R,R1 = H, OH; B = purine or pyrimidine nucleobase) were stereospecifically synthesized as virucides. Thus, I [R = R1 = H, B = cytosine, 5-fluorocytosine (II)] was prepared from L-xylose via stereoselective glycosidation of 1,2-di-O-acetyl-3,5-di-O-benzoyl-L-xylofuranose with uracil. These compds., and particularly II, showed a strong **antiviral** activity (ED50 = 3×10^{-7} M).

IC ICM C07H019-04
ICS A61K031-70; C07D405-04; C07D473-00; A61K031-505; A61K031-52

CC 33-9 (Carbohydrates)
Section cross-reference(s): 1

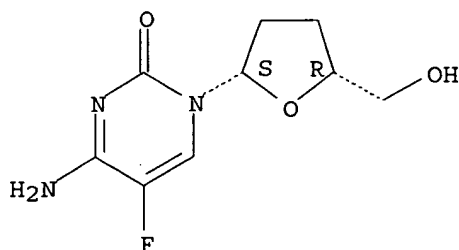
IT 121154-51-6P **147058-39-7P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of dideoxyblpentafuranonucleosides as virucides via stereoselective glycosidation of xylofuranose with uracil)

IT **147058-39-7P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of dideoxyblpentafuranonucleosides as virucides via stereoselective glycosidation of xylofuranose with uracil)

RN 147058-39-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L69 ANSWER 19 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:858026 HCAPLUS

DOCUMENT NUMBER: 124:215

TITLE: L- and D-enantiomers of 2',3'-dideoxycytidine 5'-triphosphate analogs as substrates for human DNA polymerases. Implications for the mechanism of toxicity

AUTHOR(S): Kukhanova, Marina; Liu, Shwu-Huey; Mozzherin, Dmitry; Lin, Tai-Shun; Chu, Chung K.; Cheng, Yung-Chi

CORPORATE SOURCE: Dep. Pharmacology, Yale Univ. Sch. Med., New Haven, CT, 06510, USA

SOURCE: Journal of Biological Chemistry (1995), 270(39), 23055-9

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 5'-Triphosphates of β -D and β -L-enantiomers of 2',3'-dideoxycytidine (ddC), 2',3'-dideoxy-5-fluorocytidine (FddC), 1,3-dioxolane-cytidine (OddC), and 1,3-dioxolane-5-fluorocytidine (FoddC) were evaluated as inhibitors and substrates for human DNA polymerases α , β , γ , δ , and ϵ . L-DdCTP was not a substrate or inhibitor for any DNA polymerase studied; L-FddCTP was not an inhibitor or substrate for replicative DNA polymerases and was a less potent inhibitor of DNA polymerases γ and β than its D-enantiomer by 2 orders of magnitude. In contrast, all L-dioxolane analogs were potent inhibitors and chain terminators for all cellular DNA polymerases studied. The K_i values of their 5'-triphosphates for DNA polymerase γ were found to be in the following order: DddC < D-FddC < L-OddC < L-FoddC < L-FoddC < L-FddC. The K_i values of L-OddCTP for the reactions catalyzed by DNA polymerases α , δ , ϵ , β , and γ were 6.0, 1.9, 0.4, 3.0, and 0.014 μ M, resp., and those of L-FoddCTP were 6.5, 1.9, 0.7, 19, and 0.06 μ M, resp. The K_m values for incorporation of L-OddCTP into the standing points of primer extension were also evaluated and determined to be 1.3, 3.5, 1.5, 2.8, and 0.7 μ M for DNA polymerases α , δ , ϵ , β , and γ , resp. The incorporation of dioxolane analogs into DNA by replicative DNA polymerases could explain their potent cellular toxicity.

CC 1-3 (Pharmacology)

Section cross-reference(s): 7

IT 66004-77-1 104086-76-2, 5'-Cytidylic acid, 2',3'-dideoxy-

146369-72-4 161170-31-6 170964-87-1 170964-88-2

171039-00-2 171039-01-3

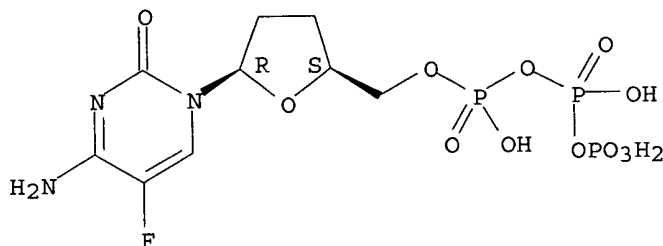
RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); BIOL (Biological study)

(enantiomers of dideoxycytidine triphosphates as substrates for human

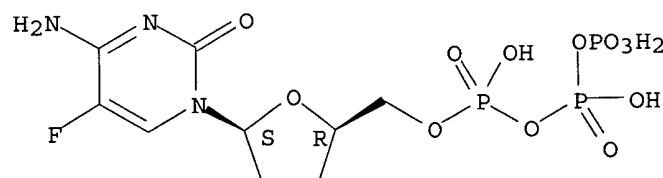
DNA polymerases; implications for mechanism of toxicity)
IT 146369-72-4 161170-31-6
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); BIOL (Biological study)
(enantiomers of dideoxycytidine triphosphates as substrates for human
DNA polymerases; implications for mechanism of toxicity)
RN 146369-72-4 HCAPLUS
CN Cytidine 5'-(tetrahydrogen triphosphate), 2',3'-dideoxy-5-fluoro- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



RN 161170-31-6 HCAPLUS
CN Triphosphoric acid, P-[(2R,5S)-[5-(4-amino-5-fluoro-2-oxo-1(2H)-pyrimidinyl)tetrahydro-2-furanyl]methyl] ester (9CI) (CA INDEX NAME)

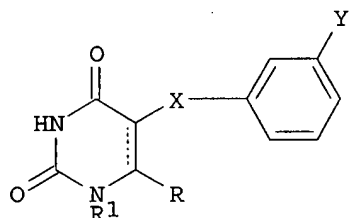
Absolute stereochemistry.



L69 ANSWER 20 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:713967 HCAPLUS
DOCUMENT NUMBER: 123:102800
TITLE: DHUDase or UrdPase inhibitors as therapeutic agents
INVENTOR(S): El Kouni, Mahmoud H.; Naguib, Fardos N. M.; Schinazi, Raymond F.
PATENT ASSIGNEE(S): UAB Research Foundation, USA
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9512400	A1	19950511	WO 1994-US11173	19940930
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5476855	A	19951219	US 1993-146838	19931102

CA 2176720	AA	19950511	CA 1994-2176720	19940930
CA 2176720	C	20060801		
AU 9478476	A1	19950523	AU 1994-78476	19940930
AU 699914	B2	19981217		
EP 725641	A1	19960814	EP 1994-929398	19940930
EP 725641	B1	20001213		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09507054	T2	19970715	JP 1995-513211	19940930
JP 3621102	B2	20050216		
AT 198046	E	20001215	AT 1994-929398	19940930
ES 2155093	T3	20010501	ES 1994-929398	19940930
PT 725641	T	20010531	PT 1994-929398	19940930
US 5721241	A	19980224	US 1995-466470	19950606
US 37623	E	20020402	US 1997-980629	19971201
PRIORITY APPLN. INFO.:			US 1993-146838	A 19931102
			WO 1994-US11173	W 19940930
OTHER SOURCE(S):		MARPAT 123:102800		
GI				



I

AB Compds., I (X = S, Se; Y = I, F, Cl, Br, methoxy, benzyl, selenylphenyl, thiophenyl; R = H, O; R1 = H, acyclo), effective in inhibition of dihydrouracil dehydrogenase (DHUDe) or (uridine phosphorylase) UrdPase are provided. The compds. can be used in pharmaceutical compns., along with various chemotherapeutic agents to increase the efficacy of the treatment. These compds. can also be used in methods of treating patients by co-administering or sequentially administering the enzyme inhibiting compds. with a chemotherapeutic agent effective to treat cancers, or viral, fungal, bacterial, or parasitic infections. The compds. have further utility in enhancing imaging. They can also be administered alone to prevent and/or treat disorders of pyrimidine catabolism and other physiol. disorders.

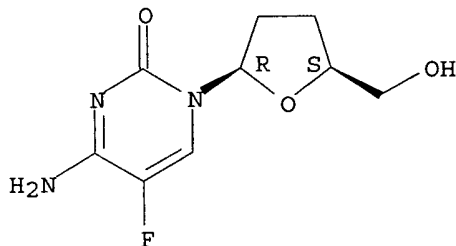
IC ICM A61K031-515
ICS A61K031-505; C07D239-02; C07D401-00

CC 1-12 (Pharmacology)
Section cross-reference(s): 28, 63

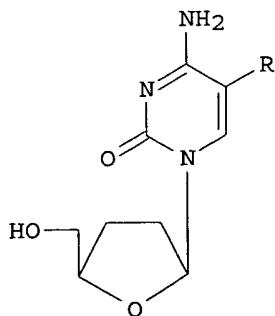
IT 50-91-9, 5-Fluoro-2'-deoxyuridine 51-21-8, 5-Fluorouracil 2022-85-7, 5-Fluorocytosine 3056-17-5 3094-09-5, 5'-Deoxy-5-fluorouridine 7481-88-1, 2',3'-Dideoxycytidin-2'-ene 17902-23-7, 1-(2-Tetrahydrofuryl)-5-fluorouracil 25526-93-6, 3'-Fluoro-3'-deoxythymidine 30516-87-1, 3'-Azido-3'-deoxythymidine 57610-22-7, 1-Ethoxymethyl-5-fluorouracil 84472-85-5, 3'-Azido-2',3'-dideoxyuridine 107036-62-4, 5-Fluoro-2',3'-dideoxycytidine 143491-54-7, 2',3'-Dideoxy-5-fluoro-3'-thiacytidine 148551-09-1 153080-96-7 165672-23-1 165672-24-2 165672-25-3 165672-26-4 165672-27-5 165672-28-6 165672-29-7 165672-30-0

RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(therapeutic compns. containing inhibitors of dihydrouracil dehydrogenase
and uridine phosphorylase)
IT 107036-62-4, 5-Fluoro-2',3'-dideoxycytidine
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(therapeutic compns. containing inhibitors of dihydrouracil dehydrogenase
and uridine phosphorylase)
RN 107036-62-4 HCAPLUS
CN Cytidine, 2',3'-dideoxy-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L69 ANSWER 21 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:631048 HCAPLUS
DOCUMENT NUMBER: 123:314336
TITLE: 2'-And/or 3'-deoxy- β -L-pentofuranosyl nucleoside
derivatives: stereospecific synthesis and
antiviral activities
AUTHOR(S): Gosselin, Gilles; Mathe, Christophe; Bergogne,
Marie-Christine; Aubertin, Anne-Marie; Kirn, Andre;
Sommadosi, Jean-Pierre; Schinazi, Raymond; Imbach,
Jean-Louis
CORPORATE SOURCE: Laboratoire Chimie Bio-organique, Univ. Montpellier
II, Montpellier, 34095, Fr.
SOURCE: Nucleosides & Nucleotides (1995), 14(3-5), 611-17
CODEN: NUNUD5; ISSN: 0732-8311
PUBLISHER: Dekker
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB Several L-enantiomers of nucleoside analogs I (R = H, F) were

stereospecifically synthesized by a multi-step reaction from L-xylose and their **antiviral** properties were examined in vitro. Two of them, namely β -L-2',3'-dideoxycytidine (β -L-ddC) and its 5-fluoro derivative (β -L-FddC) were found to have potent anti-human immunodeficiency virus (HIV) and significant antihepatitis B virus (HBV) activities in cell cultures.

CC 33-9 (Carbohydrates)

Section cross-reference(s): 1

IT Asymmetric synthesis and induction

Virucides and Virustats

(asym. synthesis and **antiviral** activity of deoxy-L-pentofuranosyl nucleosides)

IT Nucleosides, preparation

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(asym. synthesis and **antiviral** activity of deoxy-L-pentofuranosyl nucleosides)

IT 121154-51-6P 147058-39-7P

RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(asym. synthesis and **antiviral** activity of deoxy-L-pentofuranosyl nucleosides)

IT 51-21-8, 5-FluoroUracil 66-22-8, Uracil, reactions 609-06-3, L-Xylose

RL: RCT (Reactant); RACT (Reactant or reagent)

(asym. synthesis and **antiviral** activity of deoxy-L-pentofuranosyl nucleosides)

IT 28616-91-3P 114861-22-2P 166411-39-8P 166411-43-4P 169823-49-8P
169823-50-1P 169823-51-2P 169823-52-3P 169823-53-4P 170079-20-6P
170079-21-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(asym. synthesis and **antiviral** activity of deoxy-L-pentofuranosyl nucleosides)

IT 147058-39-7P

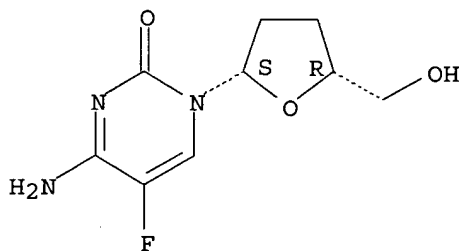
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(asym. synthesis and **antiviral** activity of deoxy-L-pentofuranosyl nucleosides)

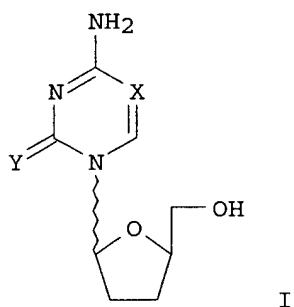
RN 147058-39-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L69 ANSWER 22 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1995:353510 HCAPLUS
 DOCUMENT NUMBER: 122:240323
 TITLE: Synthesis of several pyrimidine L-nucleoside analogs
 as potential **antiviral** agents
 AUTHOR(S): Lin, Tai-Shun; Luo, Mei-Zhen; Liu, Mao-Chin
 CORPORATE SOURCE: Sch. Med., Yale Univ., New Haven, CT, 06520-8066, USA
 SOURCE: Tetrahedron (1995), 51(4), 1055-68
 CODEN: TETRAB; ISSN: 0040-4020
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



- AB β -L-5-Iodo-2'-deoxyuridine (β -L-IUdR) and 1-[(β -L-arabinofuranosyl)-E-5-(2-bromovinyl)]uracil (β -L-BV-ara-U) have been synthesized via a multi-step synthesis from L-arabinose. Dideoxy- β -L-nucleosides, e.g. I (X = N, Y = O; X = S, Y = CH), were synthesized by direct coupling of 1-O-acetyl-5-O-(tert-butyldimethylsilyl)-2,3-dideoxy-L-ribofuranose with the corresponding silylated bases, in the presence of EtAlCl₂ in CH₂Cl₂, followed by separation of the α - and β -isomers and deblocking of the 5'-protecting groups. In addition, 2',3'-dideoxy- β -L-5-fluorocytidine, a potent anti-HIV and anti-HBV agent, was synthesized by an alternative methodol. from 2',3'-dideoxy- β -L-5-fluorouridine via a 4-triazolylpyrimidinone intermediate. These L-nucleoside analogs were tested in vitro against HIV, HBV, HSV-1, and intermediate. These L-nucleoside analogs were tested in vitro against HIV, HBV, HSV-1, and HSV-2. Among these compds., 2',3'-dideoxy- β -L-5-azacytidine was found to show significant activity against HBV in vitro at approx. the same level as 2',3'-dideoxy- β -D-cytidine (ddC), which is known potent anti-HBV agent.
- CC 33-9 (Carbohydrates)
 Section cross-reference(s): 1
- IT Virucides and Virustats
 (synthesis and **antiviral** activity of of pyrimidine L-nucleoside analogs)
- IT Nucleosides, preparation
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (synthesis and **antiviral** activity of of pyrimidine L-nucleoside analogs)
- IT 162239-34-1P 162239-35-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and **antiviral** activity of of pyrimidine
L-nucleoside analogs)

IT 107036-52-2P **147058-39-7P** 162106-25-4P 162239-38-5P
162239-41-0P 162239-42-1P 162239-43-2P 162239-48-7P 162239-49-8P
162239-50-1P

RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); SPN (Synthetic preparation); BIOL
(Biological study); PREP (Preparation)
(synthesis and **antiviral** activity of of pyrimidine
L-nucleoside analogs)

IT 931-86-2, 5-Azacytosine 31501-19-6 31501-46-9 126637-93-2
153506-50-4

RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and **antiviral** activity of of pyrimidine
L-nucleoside analogs)

IT 40093-89-8P, 1-(β -L-Arabinofuranosyl)uracil 153506-49-1P
162106-23-2P 162106-24-3P 162239-36-3P 162239-37-4P 162239-39-6P
162239-40-9P 162239-44-3P 162239-45-4P 162239-46-5P 162239-47-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(synthesis and **antiviral** activity of of pyrimidine
L-nucleoside analogs)

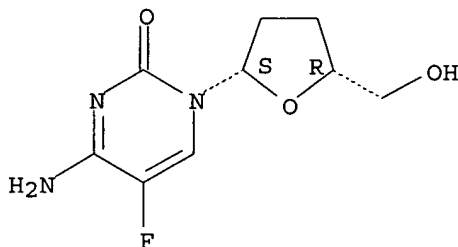
IT **147058-39-7P**

RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); SPN (Synthetic preparation); BIOL
(Biological study); PREP (Preparation)
(synthesis and **antiviral** activity of of pyrimidine
L-nucleoside analogs)

RN 147058-39-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-
(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L69 ANSWER 23 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:347121 HCAPLUS

DOCUMENT NUMBER: 122:123093

TITLE: L-2-O,3-O-dideoxy nucleoside analogs as antihepatitis
B (hbv) and anti-HIV agents

INVENTOR(S): Lin, Tai-Shun; Cheng, Yung-Chi

PATENT ASSIGNEE(S): Yale University, USA

SOURCE: PCT Int. Appl., 54 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9427616	A1	19941208	WO 1994-US5790	19940523
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5627190	A	19970506	US 1993-98650	19930728
CA 2163520	AA	19941208	CA 1994-2163520	19940523
CA 2163520	C	20060110		
AU 9470430	A1	19941220	AU 1994-70430	19940523
AU 693795	B2	19980709		
EP 707481	A1	19960424	EP 1994-919207	19940523
EP 707481	B1	20000816		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08510747	T2	19961112	JP 1995-500872	19940523
AT 195423	E	20000915	AT 1994-919207	19940523
US 5830881	A	19981103	US 1996-724138	19960930
HK 1013257	A1	20010202	HK 1998-114607	19981222
GR 3034379	T3	20001229	GR 2000-402067	20000908
PRIORITY APPLN. INFO.:				US 1993-67299 A 19930525
				US 1993-98650 A 19930728
				WO 1994-US5790 W 19940523
				US 1995-456635 A3 19950601

OTHER SOURCE(S): MARPAT 122:123093

AB The present invention relates to the discovery that certain dideoxynucleoside analogs which contain a dideoxy ribofuranosyl moiety having an L-configuration (as opposed to the naturally occurring D-configuration) exhibit unexpected activity against Hepatitis B virus (HBV). In particular, the compds. according to the present invention show potent inhibition. of the replication of the virus in combination with very low toxicity to the host cells (i.e., animal or human tissue). Compds. according to the present invention exhibit primary utility as agents for inhibiting the growth or replication of HBV, HIV and other retroviruses, most preferably HBV. The compound 1-(2,3-dideoxy-beta-L-ribofuranosyl)-5-fluorocytosine is shown to be a potent anti-HIV agent with low toxicity to host cells.

IC ICM A61K031-70

ICS C07H019-00

CC 1-5 (Pharmacology)

Section cross-reference(s): 33

IT 61246-68-2P 107036-57-7P 121154-51-6P 135212-57-6P
 147058-39-7P 153547-98-9P 158850-64-7P 160853-25-8P
 160853-27-0P 160853-28-1P 160853-29-2P 160853-30-5P 160853-31-6P
 160853-32-7P 160853-33-8P 160853-34-9P 160853-35-0P 160853-36-1P
 160853-37-2P 160853-38-3P 160853-39-4P 160853-40-7P 160853-41-8P
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 160963-15-5P 160963-16-6P 160963-17-7P 160963-18-8P
 160963-19-9P 160963-20-2P 160982-27-4P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)

(dideoxy nucleoside analogs as antihepatitis B and anti-HIV agents)

IT 107036-57-7P 147058-39-7P 160963-15-5P
160963-16-6P

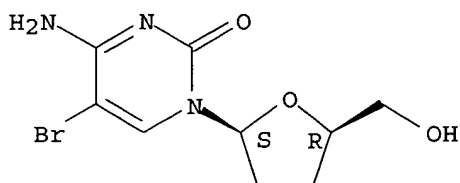
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(dideoxy nucleoside analogs as antihepatitis B and anti-HIV agents)

RN 107036-57-7 HCAPLUS

CN Cytidine, 5-bromo-2',3'-dideoxy- (9CI) (CA INDEX NAME)

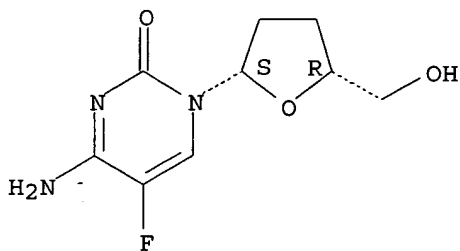
Absolute stereochemistry.



RN 147058-39-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

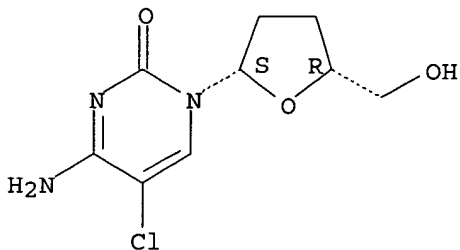
Absolute stereochemistry. Rotation (-).



RN 160963-15-5 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-chloro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

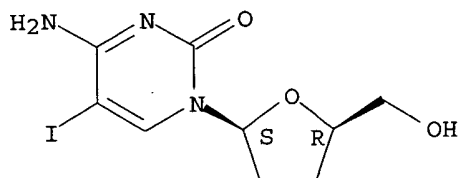


RN 160963-16-6 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-iodo-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-

2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L69 ANSWER 24 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:104909 HCAPLUS

DOCUMENT NUMBER: 122:154909

TITLE: Inhibition of human immunodeficiency virus type 1 reverse transcriptase by the 5'-triphosphate β enantiomers of cytidine analogs

AUTHOR(S): Faraj, Abdesslem; Agrofoglio, Luigi A.; Wakefield, John K.; McPherson, Sylvia; Morrow, Casey D.; Gosselin, Gilles; Mathe, Christophe; Imbach, Jean-Louis; Schinazi, Raymond F.; Sommadossi, Jean-Pierre

CORPORATE SOURCE: Cent. AIDS Res., Univ. Alabama, Birmingham, AL, 35294, USA

SOURCE: Antimicrobial Agents and Chemotherapy (1994), 38(10), 2300-5

CODEN: AMACCQ; ISSN: 0066-4804

DOCUMENT TYPE: Journal

LANGUAGE: English

AB (-)- β -L-2',3'-Dideoxycytidine (L-ddC) and (-)- β -L-2',3'-dideoxy-5-fluorocytidine (L-FddC) have been reported to be potent and selective inhibitors of human immunodeficiency virus type 1 (HIV-1) and type 2 (HIV-2) in vitro. In the present study, the 5'-triphosphates of L-ddC (L-ddCTP) and L-FddC (L-FddCTP) were demonstrated to competitively inhibit HIV-1 reverse transcriptase (RT); with inhibition consts. (K_i) of 2 and 1.6 μ M, resp., when a poly(rI)·oligo(dC)10-15 template primer was used; in comparison K_i values for β -D-2',3'-dideoxy-5-fluorocytidine 5'-triphosphate (D-FddCTP) were 1.1 and 1.4 μ M, resp. Use of the mutant RT at position 184 (substitution of methionine to valine [M184V]), which is associated with resistance to β -L-2',3'-dideoxy-3'-thiacytidine (3TC) and β -L-2',3'-dideoxy-5-fluoro-3'-thiacytidine (FTC), resulted in significant increases (50- to 60-fold) in K_i values for L-ddCTP and L-FddCTP, whereas the elevation in K_i values for D-ddCTP and D-FddCTP was moderate (2-fold). L-DdCTP and L-FddCTP did not inhibit human DNA polymerases α and β up to 100 μ M. In contrast, D-ddCTP and D-FddCTP inhibited human DNA polymerase β , with K_i values of 0.5 and 2.5 μ M, resp. By using sequencing anal., L-ddCTP and L-FddCTP exhibited DNA chain-terminating activities toward the parental HIV-1 RT, whereas they were not a substrate for the mutant M184V HIV-1 RT. L-DdC and L-FddC did not inhibit the mitochondrial DNA content of human cells up to a concentration of 10 μ M, whereas D-ddC and D-FddC decreased the mitochondrial DNA content by 90% at concns. of 1 and 10 μ M, resp.

CC 7-3 (Enzymes)

Section cross-reference(s): 1

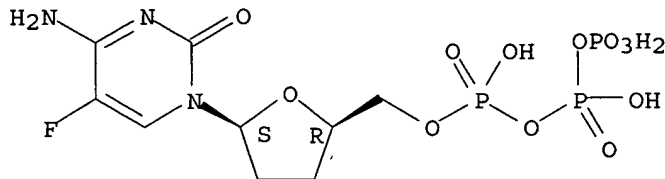
IT 7481-89-2 66004-77-1 92586-35-1 107036-62-4 121154-51-6

143188-53-8 146369-72-4 147058-39-7 161170-30-5

RN 161170-31-6 HCAPLUS

CN Triphosphoric acid, P-[(2R,5S)-[5-(4-amino-5-fluoro-2-oxo-1(2H)-pyrimidinyl)tetrahydro-2-furanyl)methyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L69 ANSWER 25 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:681051 HCAPLUS

DOCUMENT NUMBER: 121:281051

TITLE: Synthesis and biological evaluation of pyrimidine and purine α -L-2',3'-dideoxy nucleosides

AUTHOR(S): Van Draanen, Nanine A.; Koszalka, George W.

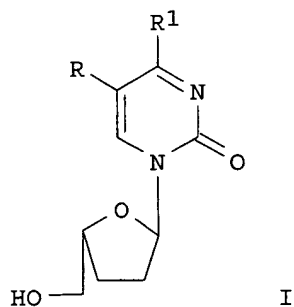
CORPORATE SOURCE: Div. Experimental Therapy, Burroughs Wellcome Co., Research Triangle Park, NC, 27709, USA

SOURCE: Nucleosides & Nucleotides (1994), 13(8), 1679-93
CODEN: NUNUD5; ISSN: 0732-8311

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB α -L-2',3'-Dideoxy nucleosides, e.g. I (R = H, Me, F, R1 = NH₂; R = Br, Cl, F, iodo, CF₃, C.tplbond.CH, R1 = OH), were prepared as potential **antiviral** agents. The pyrimidine nucleosides were prepared by standard Vorbrueggen coupling reactions. The purine analogs were prepared by enzymic transfer of the dideoxy sugar from a pyrimidine to a purine base. These compds. were inactive against HIV-1, HBV, HSV-1 and -2, VZV, and HCMV.

CC 33-9 (Carbohydrates)

Section cross-reference(s): 1, 7, 9

IT Virucides and Virustats

(preparation and **antiviral** activity of α -L-dideoxy nucleosides)

IT Nucleosides, preparation

161170-31-6

RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); BIOL (Biological study)
(HIV-1 reverse transcriptase inhibition by β enantiomers of CTP
and cytidine analogs)

IT 107036-62-4 146369-72-4 147058-39-7

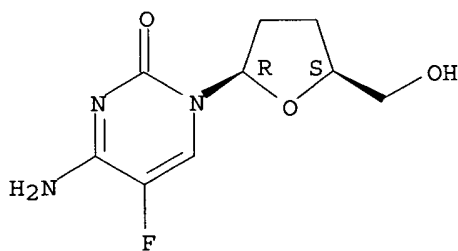
161170-31-6

RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); BIOL (Biological study)
(HIV-1 reverse transcriptase inhibition by β enantiomers of CTP
and cytidine analogs)

RN 107036-62-4 HCAPLUS

CN Cytidine, 2',3'-dideoxy-5-fluoro- (9CI) (CA INDEX NAME)

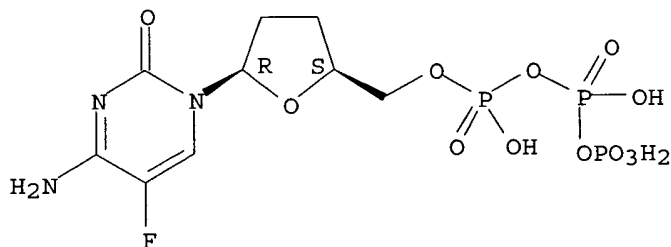
Absolute stereochemistry.



RN 146369-72-4 HCAPLUS

CN Cytidine 5'-(tetrahydrogen triphosphate), 2',3'-dideoxy-5-fluoro- (9CI)
(CA INDEX NAME)

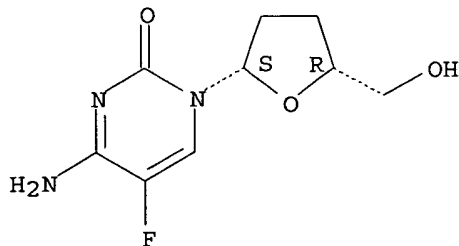
Absolute stereochemistry.



RN 147058-39-7 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation and **antiviral** activity of α -L-dideoxy nucleosides)

IT 121154-50-5P 121154-53-8P 158850-67-0P 158850-68-1P 158850-69-2P
158850-70-5P

RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation and **antiviral** activity of α -L-dideoxy nucleosides)

IT 121154-52-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(preparation and **antiviral** activity of α -L-dideoxy nucleosides)

IT 133008-04-5P **147058-40-0P** 158780-64-4P 158850-59-0P
158850-60-3P 158850-61-4P 158850-62-5P 158850-63-6P 158850-65-8P
158850-66-9P

RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation and **antiviral** activity of α -L-dideoxy nucleosides)

IT 9025-06-3, Cytidine deaminase 9030-21-1, Purine nucleoside Phosphorylase
9030-23-3, Thymidine phosphorylase

RL: CAT (Catalyst use); USES (Uses)

(preparation and **antiviral** activity of α -L-dideoxy nucleosides)

IT 71-30-7, Cytosine 554-01-8, 5-Methylcytosine 127306-45-0

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation and **antiviral** activity of α -L-dideoxy nucleosides)

IT 121154-51-6P 158850-64-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and **antiviral** activity of α -L-dideoxy nucleosides)

IT **147058-40-0P**

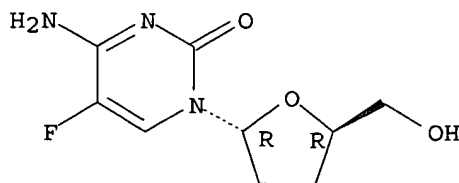
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation and **antiviral** activity of α -L-dideoxy nucleosides)

RN 147058-40-0 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[tetrahydro-5-(hydroxymethyl)-2-furanyl]-, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L69 ANSWER 26 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:671374 HCAPLUS

DOCUMENT NUMBER: 121:271374

TITLE: Effect of anti-HIV 2'- β -fluoro-2',3'-dideoxynucleoside analogs on the cellular content of mitochondrial DNA and on lactate production

AUTHOR(S): Tsai, Ching-Hwa; Doong, Shin-Lian; Johns, David G.; Driscoll, John S.; Cheng, Yung-Chi

CORPORATE SOURCE: Sch. Med., Yale Univ., New Haven, CT, 06510, USA

SOURCE: Biochemical Pharmacology (1994), 48(7), 1477-81

CODEN: BCPA6; ISSN: 0006-2952

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Many dideoxynucleosides that are effective against human immunodeficiency virus (HIV) also are potent inhibitors of mitochondrial DNA (mtDNA) synthesis, and the resulting mtDNA decrease could be responsible for the delayed clin. toxicity sometimes observed with these drugs. The following compds. have been examined for their toxicity to human lymphoid CEM cells, and their ability to suppress mtDNA content: 2',3'-dideoxycytidine (ddC), 2',3'-Dideoxyadenosine (ddA), 2',3'-dideoxyinosine (ddI) and 2',3'-dideoxyguanosine (ddG); and their 2'- β -fluoro analogs; β -F-ddC, β -F-ddA, β -F-ddI and β -F-ddG. Two other fluoro analogs, 5-F-ddC and 2'- β ,5-di-F-ddC were also examined. The ratio of C-IC₅₀ (concentration that inhibited cell growth by 50%) to mt-IC₅₀ (concentration that inhibited mtDNA synthesis by 50%) was determined for each compound

The rank-order of this ratio was ddC>5-F-ddC ddA>ddI>ddG> β -F-ddC> β -F-ddA> β -F-ddG with the highest ratios indicating the greatest potential for delayed toxicity. In comparison with ddC, β -F-ddC and β -F-ddA were 5,000 and 22,000 times less potent, resp., in suppressing cellular mtDNA content, while their anti-HIV potencies were decreased only modestly relative to their unfluorinated parent compds. β -F-ddI and 2'- β ,5-di-F-ddC produced neither cellular toxicity nor mtDNA suppression at concns. of 500 and 1000 μ M, resp. Lactic acid, the product of compensatory glycolysis that results from the inhibition of mitochondrial oxidative phosphorylation, was measured after cells were treated with these compds. There appears to be a concentration-related correlation between the increase of lactic acid and the extent of mtDNA inhibition for the compds. examined

CC 1-5 (Pharmacology)

IT 4097-22-7 7481-89-2 69655-05-6 85326-06-3 107036-62-4
110143-10-7 117525-25-4 119555-47-4 128496-09-3 156900-23-1

RL: ADV (Adverse effect, including toxicity); **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study);
USES (Uses)

(effect of anti-HIV 2'- β -fluoro-2',3'-dideoxynucleoside analogs on the cellular content of mitochondrial DNA and on lactate production)

IT 107036-62-4

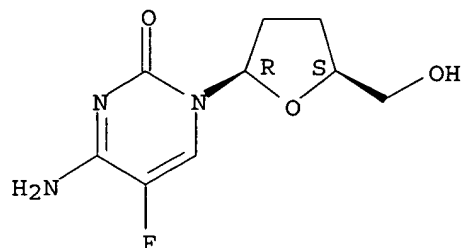
RL: ADV (Adverse effect, including toxicity); **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study);
USES (Uses)

(effect of anti-HIV 2'- β -fluoro-2',3'-dideoxynucleoside analogs on the cellular content of mitochondrial DNA and on lactate production)

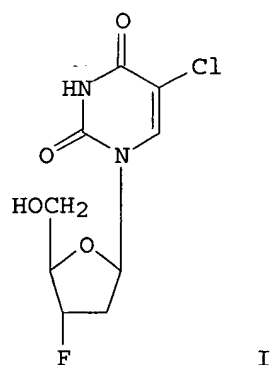
RN 107036-62-4 HCAPLUS

CN Cytidine, 2',3'-dideoxy-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L69 ANSWER 27 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:441201 HCAPLUS
DOCUMENT NUMBER: 113:41201
TITLE: Synthesis and anti-HIV evaluation of
2',3'-dideoxyribo-5-chloropyrimidine analogs: reduced
toxicity of 5-chlorinated 2',3'-dideoxynucleosides
AUTHOR(S): Van Aerschot, Arthur; Everaert, Dirk; Balzarini, Jan;
Augustyns, Koen; Jie, Liu; Janssen, Gerard; Peeters,
Oswald; Blaton, Norbert; De Ranter, Camiel; et al.
CORPORATE SOURCE: Rega Inst. Med. Res., Kathol. Univ. Leuven, Louvain,
B-3000, Belg.
SOURCE: Journal of Medicinal Chemistry (1990), 33(6), 1833-9
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 113:41201
GI



AB In view of the selective anti-HIV activity of 2',3'-dideoxy-3'-fluoro-5-chlorouridine (I), a series of eight 2',3'-dideoxy-5-chloropyrimidines were synthesized and evaluated for their inhibitory activity against human immunodeficiency virus type 1 (HIV-1) replication in MT-4 cells. A marked improvement in selectivity was noted for the 5-chlorouracil derivs. of 2,3-dideoxyribofuranose, 3-azido-2,3-dideoxyribofuranose, and 3-fluoro-2,3-dideoxyribofuranose, mainly due to decreased toxicity of the compds. for the host cells. While chlorination of 2',3'-dideoxycytidine removed the anti-HIV activity, introduction of Cl at C(5) of 3'-fluoro-, 3'-azido- or 2',3'-didehydro-2',3'-dideoxycytidine led to reduced

cytotoxicity with only slightly reduced anti-HIV activity. X-ray anal. revealed no close resemblance of I to 3'-azido-3'-deoxythymidine (AZT).

CC 33-9 (Carbohydrates)

Section cross-reference(s): 1, 75

IT 3056-17-5P 108441-51-6P 119644-22-3P 124743-30-2P
124743-31-3P 127492-31-3P 127492-32-4P 127492-36-8P
 127516-98-7P 127592-40-9P

RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (preparation and **antiviral** activity of)

IT 120815-05-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (preparation, attempted amination, and **antiviral** activity of)

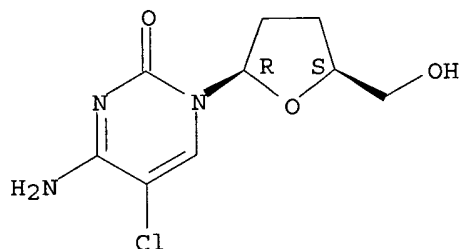
IT **124743-31-3P**

RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (preparation and **antiviral** activity of)

RN 124743-31-3 HCAPLUS

CN Cytidine, 5-chloro-2',3'-dideoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L69 ANSWER 28 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1990:48297 HCAPLUS

DOCUMENT NUMBER: 112:48297

TITLE: 2',3'-Didehydro-2',3'-dideoxy-5-chlorocytidine is a selective anti-retrovirus agent

AUTHOR(S): Balzarini, Jan; Van Aerschot, Arthur; Herdewijn, Piet; De Clercq, Erik

CORPORATE SOURCE: Rega Inst. Med. Res., Kathol. Univ. Leuven, Louvain, B-3000, Belg.

SOURCE: Biochemical and Biophysical Research Communications (1989), 164(3), 1190-7
 CODEN: BBRCA9; ISSN: 0006-291X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 2',3'-Didehydro-2',3'-dideoxy-5-chlorocytidine (D4CC) is, in contrast with 2',3'-dideoxy-5-chlorocytidine (ddClCyd) and 2',3'-dideoxy-5-chlorouridine (D4CU), a potent and selective inhibitor of the replication of human immunodeficiency virus (HIV) types 1 and 2, simian immunodeficiency virus (SIV) and simian AIDS-related virus (SRV). D4CC is a poor inhibitor of the phosphorylation of [5-3H]2'-deoxycytidine (dCyd) by partially purified MT-4 cell dCyd kinase (Ki: 612 μ M). The findings

that (i) D4CC has little, if any, affinity for MT-4 cell Cyd/dCyd deaminase, (ii) D4CU is not **antivirally** active and (iii) the antiretroviral action of D4CC can be reversed by dCyd, but not dThd, indicate that D4CC is **antivirally** active as its Cyd metabolite (D4CC 5'-triphosphate) and does not need to be deaminated (to the corresponding Urd metabolite) to exert its antiretroviral action.

CC 1-5 (Pharmacology)

IT 7481-89-2 120815-05-6 124743-30-2 124743-31-3

RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study) (antiretroviral action of)

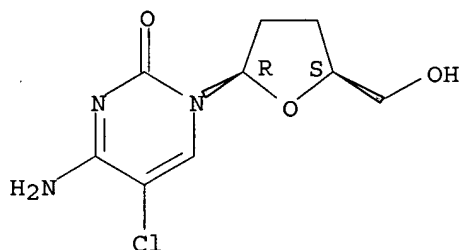
IT 124743-31-3

RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study) (antiretroviral action of)

RN 124743-31-3 HCAPLUS

CN Cytidine, 5-chloro-2',3'-dideoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L69 ANSWER 29 OF 29 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1989:458275 HCAPLUS

DOCUMENT NUMBER: 111:58275

TITLE: 5-Substituted-2',3'-dideoxycytidine compounds with anti-HTLV-III activity

INVENTOR(S): Driscoll, John S.; Marquez, Victor E.; Kim, Chong Ho; Kelley, James A.

PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA

SOURCE: U.S., 7 pp.

CODEN: USXXAM

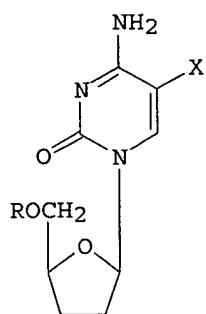
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 4788181	A	19881129	US 1986-913575	19860929
PRIORITY APPLN. INFO.:			US 1986-913575	19860929
OTHER SOURCE(S):		CASREACT 111:58275; MARPAT 111:58275		
GI				



I

AB The title compds. [I; R = H, Na2O3P; X ; F, Br], useful as inhibitors of HIV pathogens, are prepared 2',3'-Dideoxycytidine was brominated with N-bromosuccinimide to give 57% 2',3'-dideoxy-5-bromocytidine, which showed 6% protective effect against HTLV-III/LAV pathogenesis at 1 µM with 14% cytotoxicity vs. 3% protective effect at 10 µM with 8% cytotoxicity for 2',3'-dideoxycytidine.

IC ICM A61K031-70
ICS C07H019-06; C07H019-10

INCL 514049000

CC 33-9 (Carbohydrates)
Section cross-reference(s): 1

ST halodideoxycytidine deriv prepn **antiviral**; cytidine halodideoxy deriv prepn **antiviral**; HTLV III virus inhibitor halodideoxycytidine deriv; fluorodideoxycytidine deriv **antiviral**; bromodideoxycytidine deriv **antiviral**; phosphorylated dideoxycytidine deriv **antiviral**

IT 107132-15-0 107133-41-5 121590-63-4 121590-64-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**antiviral** activity of)

IT 7791-71-1P 107036-45-3P 107036-46-4P 107036-47-5P 107036-48-6P
107036-51-1P 107036-53-3P 107036-55-5P 107036-58-8P 107036-59-9P
107036-60-2P 107036-61-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of **antiviral** nucleosides)

IT 107036-52-2P 107036-56-6P 107036-57-7P, 5-Bromo-2',3'-dideoxycytidine 107036-62-4P, 5-Fluoro-2',3'-dideoxycytidine
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as **antiviral** agent)

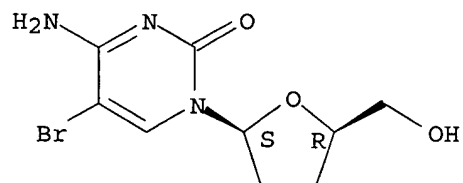
IT 50-91-9, 2'-Deoxy-5-fluorouridine 288-88-0, 1H-1,2,4-Triazole 3282-30-2, Pivaloyl chloride 6160-65-2, 1,1'-Thiocarbonyldiimidazole 7481-89-2, 2',3'-Dideoxycytidine
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of **antiviral** nucleosides)

IT 107036-57-7P, 5-Bromo-2',3'-dideoxycytidine 107036-62-4P, 5-Fluoro-2',3'-dideoxycytidine
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as **antiviral** agent)

RN 107036-57-7 HCAPLUS

CN Cytidine, 5-bromo-2',3'-dideoxy- (9CI) (CA INDEX NAME)

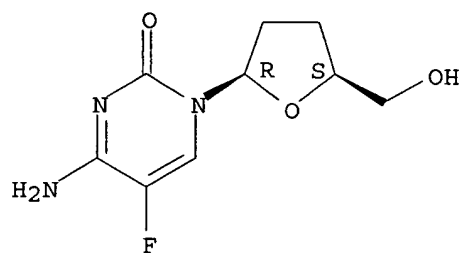
Absolute stereochemistry.



RN 107036-62-4 HCAPLUS

CN Cytidine, 2',3'-dideoxy-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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